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ACTA RADIOLOGICA
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RENAL FUNCTION FOLLOWING AORTOGRAPHY CARRIED OUT UNDER GANGLIONIC BLOCK

by

Herman Lodin and *Lars Thorén*

Attention has been drawn to the value of aortography in investigating renal lesions and certain vascular diseases when other means fail. The indications for this investigation have been discussed by a number of clinicians (BURNS and HENDON; DOSS; HARVARD; MELICK and VITT; OLLE OLSSON; REAGAN; SANTE; SMITH et coll.; WAGNER; WEYDE; and others). The risk and discomfort caused to the patient by the examination sometimes influences the investigator in his selection.

Of greatest interest is the possible damage to parenchymatous organs, notably the liver and kidneys, due to toxic or allergic reactions to the contrast medium (ALWALL et coll. 1954) or to trauma resulting from rise in pressure in the aorta when the injection is made (MILLER et coll. 1954). MELICK and VITT published in 1948 a review of 3,000 cases from the literature, among which no death directly attributable to the procedure occurred. Since then, several series have been published, none of them showing complications of importance (BURNS and HENDON — 300 cases, DENSTAD — 97, HARVARD — 100, SMITH et coll. — 300, and WEYDE — 210).

In recent years, however, reports have appeared of renal damage following aortography, mostly in isolated cases. In 1954, MILLER et coll. reported 7 cases of renal damage following 250 examinations. Of these, 4 developed reversible renal failure after the injection of 50 to 100 ml Diodrast 70 % by means of a gas pressure machine; all recovered completely after periods of oliguria lasting 10 to 11 days. The other 3 cases suffered unilateral damage considered to be due to forceful injection with a mechanical injector directly into the renal artery or an aberrant vessel; one of these developed an atrophic kidney, and, a second, a temporarily non-functioning kidney with hypertension which reverted to normal within three months. Pressure and volume are interrelated factors, the

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medium causing damage by being forced out of the capillaries, a delayed nephrographic effect being produced. These findings were confirmed in experiments in dogs. Contrast media and Indian ink were injected with great force into the exposed left renal artery, or into the aorta occluded just below the renal arteries. Radiologic and microscopic examination of the kidney revealed subcapsular and interstitial extravasation. In order that the delayed effect might be studied, a similar injection was made and the kidney left *in situ*; at the end of three weeks microscopic examination showed patchy areas of interstitial fibrosis.

Renal lesions of the lower nephron nephrosis type following aortography were reported by JOHNSSON and NORRMAN (1954), who described a case of a 63-year-old woman in whom oliguria and azotaemia developed (with normal non-protein nitrogen (NPN) not until 4 weeks after aortography). Among 32 aortographies, THOMSEN and HANSEN (1954) had 3 cases of renal damage. Two of the patients exhibited a transient rise in the NPN for some days. The third developed oliguria leading to death 11 days after the procedure. An examination two months before the investigation had shown the NPN to be normal, but a clearance test had indicated diminished renal function and preliminary intravenous urography poor excretion. Endarteritic changes were found in the kidneys and other organs at necropsy. In these cases, Diodrast 70 % had been employed, 30 to 60 ml being injected with a pressure syringe.

In order to obtain a proper idea of renal function after aortography, however, it is not enough to record only those cases in which the damage is so great that oliguria and azotaemia supervene. Renal function tests in connexion with aortography have hitherto been performed by only a few authors. LARSSON and PALMLÖV (1952) examined a series of 52 cases. In one patient with a small mobile left kidney, in whom the contrast medium was injected almost exclusively into the right renal artery, there was temporarily diminished renal function as shown by urea clearance estimations. TRAUTNER and PAHLE (1954) examined the renal function of 9 cases 72 hours before and 72 hours following aortography: no marked alteration in renal function was noted, but in several cases the endogenous creatinine clearance was found to be raised.

LINDGREN introduced in 1953 the technique of aortography under anaesthesia with hypotension, the blood-pressure being reduced to about 85 mm Hg with a barbiturate (Narkotal), and the contrast medium injected with a pressure syringe. The advantage of hypotension is a good nephrographic effect.

We wished to avoid general anaesthesia. In order to obtain the advantages of LINDGREN's procedure, we performed ganglionic block using tetra-ethyl ammonium bromide (Etamonin, Astra) with the patient

conscious and co-operative. (For a review of the pharmacology of the tetra-ethyl ammonium compounds, see MOE and FREYBURGER 1950.)

During hypotension induced in this way the state of the circulation in the vital organs is of great interest. A fall in arteriolar tonus takes place due to an interruption of the vasoconstrictor pathways (ACHESON and MOE 1946), with the result that the pressure needed to maintain the circulation in the organ diminishes. WICKBOM (1950) noted that the renal excretion of a contrast medium ceases when the blood-pressure falls to about 70 mm Hg, the filling of the capillaries remaining normal.

AAS and BLEGEN (1949) have shown that tetra-ethyl ammonium bromide produces a significant fall in the renal blood-flow and glomerular filtration rate despite only a moderate fall in blood-pressure. These effects they attribute to renal vasoconstriction. The renal circulatory resistance however shows no increase (HOOBLER et coll.). HOOBLER (1950) suggested that the diminution in the renal circulation may be purely passive, *i. e.* that the kidney is not subject to the same neurogenic vasoconstrictor tone as the arterioli in other parts of the body. The initial fall in flow is limited to the first 10 to 15 minutes, after which it returns to or approaches the original level, even if the blood-pressure remains low (MOE et coll.). EVANS and ENDERBY (1952) have compared the incidence of proteinuria and the appearance of red cells and casts in the urine in a series of 50 patients who were anaesthetized without hypotension with the same features in a similar series receiving the same type of anaesthesia but with hexamethonium and a hypotension of 55 to 80 mm Hg. There was a slightly higher incidence in the latter series, but the difference was not statistically significant. MILES et coll. (1952) found a considerable fall in renal blood-flow and glomerular filtration rate during anaesthesia, but an insignificant change when hypotension (pentamethonium) was superimposed. MCQUEEN (1952) showed that in patients with good renal function even a considerable fall in blood pressure produced by hexamethonium bromide is accompanied by no more than a transient fall in glomerular filtration rate and renal plasma flow. In patients with poor renal function a severe fall in blood-pressure produces severe and prolonged functional impairment. No clinical signs of renal damage were seen by JAMES et coll. (1953). SCHWALB (1954) reported reduction in renal function in proportion to the fall in blood-pressure after injection of hexamethonium bromide in hypertonic subjects. The renal function rose to normal again after the effect of the ganglionic block had passed off or was interrupted by administration of a drug.

According to BROMAGE (1952) and SCHWEIZER (1953), 60 mm Hg seems to be the critical level; below this the liver is impaired.

If hypotension is used in combination with the 'head-up' position the cerebral circulation is not always sufficient to prevent a minor degree

of anoxia, as shown by NILSSON (1953), VAN BERGEN et coll. (1954) and FINNERTY et coll. (1954).

No electrocardiographic signs of coronary ischaemia were found in either young or old patients in whom the pressure was reduced to 60 or 70 mm Hg (FINNERTY et coll.; JAMES et coll.; LYONS et coll.; SWERDLOW and WADE). Slight electro-cardiographic changes have in fact been reported (DAVISON 1951).

All agree that the danger of anoxia in vital organs is much greater if the blood-pressure is allowed to fall below 80 to 70 mm Hg (GRAY; HAMPTON and LITTLE).

The before-mentioned authors discuss the circulation during induced hypotension under anaesthesia. Hypotension in connexion with aortography lasts only a very few minutes instead of several hours, and furthermore the blood-pressure is not reduced to the low level of 60 to 80 mm Hg, usual in anaesthesia hypotension.

Hypotension under anaesthesia is brought about partly by ganglionic block and partly by means of the 'head-up' position so that a part of the circulating blood collects in the lower parts of the body. Our technique consists solely of ganglionic block with the patient in the horizontal position (the head not being raised). This is similar to the technique used in diagnosing peripheral vascular lesions (BERRY et coll.; LARSSON and FRISK; LYONS et coll.) or in the assessment of a patient before sympathectomy for hypertension (LYONS et coll.); most of the danger of hypotension induced during anaesthesia is thus eliminated.

The choice of a ganglion-blocking agent is of secondary importance, but we would stress the need for familiarity in the use of the drug employed.

After using ganglionic block in 40 aortographies without complication, we encountered a case of temporary renal failure, which focused our attention on renal function in relation to this procedure.

Case history

(Surg. J. 930/54.) 56-year-old man, previously healthy, complaining of vague abdominal discomfort. Expanding lesion in the lower pole of the left kidney revealed by urography. Urine: Heller's test negative, sediment contained isolated leucocytes. Blood: Sedimentation rate 7, NPN 28.

Aortography by means of a catheter introduced via the femoral artery was performed to map out the lesion, 40 ml Umbradil 70 % being injected with a pressure syringe. Before the injection the blood-pressure had been reduced from 130 to 100 mm Hg with the aid of Etamonin, afterwards being rapidly restored by means of ephedrine.

Aortography revealed the presence of a hypernephroma in the lower pole of the left kidney.

There was oliguria during the days following aortography (1st 24 hrs 400 ml, 2nd and 3rd 24 hrs periods 50 ml), after which the quantity of urine increased by degrees to

1,500 ml on the 8th day after the procedure. The non-protein nitrogen rose to 110 on the 5th day, later falling successively. Urine: Heller's test positive; Esbach's (max.) 0.7; specific gravity low — about 1.004; sediment contained a few leucocytes and solitary red cells. The patient gained about 5.4 kg in weight during the week following the investigation.

During the next two weeks, large quantities of urine were excreted — about 2,500 ml daily.

Water-tolerance tests showed diminished powers of dilution and concentration (1.009 to 1.017). Three weeks after the procedure, the non-protein nitrogen was down to 46.

Left nephrectomy was performed (L. T.) 4 weeks after aortography, a hypernephroma the size of an orange being found in the lower pole of the kidney. There were no signs of local or venous spread.

The post-operative course was uneventful. The non-protein nitrogen rose to 54 during the first days, after which it fell to normal (34 on the 10th day). There was no fluid-retention, and the urinary excretion was satisfactory (600 to 1,000 ml). The patient was discharged fit.

At follow-up examination 7 months after operation, the patient was well. Urine: about 1,000 ml per day; specific gravity 1.014; NPN 35; no albumin; sediment normal. Sedimentation rate 6. Inulin clearance 54 ml/hr. PAH clearance 217 ml/hr. Renal circulation 433 ml/hr.; filtration factor 0.25.

Liver function tests gave normal values. Serum bicarbonate 28 mEq, chlor: 100 mEq; total protein 6.4 g/100 ml.

For comparison may be mentioned HOGEMAN's (1948) findings in a group of patients aged 30 or more, treated by nephrectomy. Inulin clearance 68.3 ± 4.9; Diodrast clearance 249.1 ± 23.3; renal circulation 446 ± 46.7 and filtration factor 0.28 ± 0.016. These estimations were made at follow-up examinations at an average of 8 years after operation.

Present technique

The catheter is introduced into the femoral artery by percutaneous puncture under local anaesthesia, as described by SELDINGER. Alternatively, translumbar puncture of the aorta is made in cases in which the catheter has failed to enter the aorta owing to sinuous iliac arteries; in such cases the position of the needle in relation to the aortic wall has been checked with the aid of a stylet.

Morphine and scopolamine are administered one hour before the examination. About 10 minutes before the injection of the contrast medium, the patient receives 25 to 75 mg of pethidine intravenously, no further analgesia being used. Oxygen is administered during the procedure.

Ganglionic block is brought about before the injection of the contrast medium by means of tetra-ethyl ammonium bromide. The injection is carried out slowly at the rate of 50 to 100 mg/min. In hypertensive patients the blood-pressure is allowed to fall to between 100 and 120 mm Hg. In normotensive subjects the blood-pressure does not always fall so much during ganglionic block in the horizontal position; in such patients we usually have not allowed the systolic pressure to fall below 80 to 90 mm Hg. As a rule the dose has not exceeded 5 to 7 mg/kg body-weight. In some of the cases this dose does not reduce the blood-pressure so effectively, but we consider the effect to be satisfactory. Immediately after the injection of the contrast medium the blood-pressure is rapidly

restored with small injections of ephedrine; the original level once being reached, it is maintained. The period during which the blood-pressure is reduced as a result of the ganglionic block is about 3 minutes.

The injection of the contrast medium was formerly carried out with the aid of a pressure syringe. In the last 15 cases examined, however, it was performed manually; 30 ml Urokon 70 % were used (except in two cases in which 30 ml of Umbradil 50 % and Umbradil 70 % respectively were injected). A sensitivity test is carried out on each patient 24 hours before the investigation, 5 ml of the contrast medium being injected intravenously.

Tests of renal function. As a result of our experience with the case described above we have, since the summer of 1954, performed tests of renal function before and after all aortographies as follows.

The examination was carried out on the two days preceding aortography, and on the 1st, 2nd, 3rd and 7th days following the procedure. *Urine:* Heller's test, and, where indicated, Esbach's test. Specific gravity of the first morning specimen. Quantitative estimate of the sediment (Addie). Volume excreted in 24 hours. *Blood:* Non-protein nitrogen estimated daily. Serum protein, serum chloride and serum bicarbonate, estimated before and on the third day after the investigation. Endogenous creatinine clearance tests were also done on the two days preceding the investigation and on the 1st, 2nd, 3rd and 7th days afterwards. Blood-pressure was recorded.

Results and discussion

Renal function tests have been performed on the last 15 patients undergoing aortography under ganglionic block as described above.

The means for the various tests of renal function are almost identical before and after aortography, the red cells in the sediment alone showing a tendency to a slight increase after the procedure (this difference is, however, not statistically significant). The means for endogenous creatinine clearance showed approximately the same value before and after aortography, a slight fall however being seen in three cases (with cystic kidneys) from 57.8 to 48.1, from 80.9 to 70.3 and from 85.4 to 65.8 respectively, after the investigation. On the other hand a slight rise was seen in three cases. One of these had a unilateral tuberculous kidney and the endogenous creatine clearance rose from 55.2 to 73.4. The second was a case of carcinoma of the suprarenal gland; in this the endogenous creatine clearance rose from 50.9 to 61.1. The last case was a unilateral renal cyst with an increase from 50.5 to 79.6. Two cases in this series are of special interest: both had low creatinine clearance values from the beginning. On intravenous urography, Case 1 showed a non-functioning left kidney. (The value of the NPN was normal (33 mg %) as was the concentration ability of the kidneys (1.021) The diagnosis (acute nephritis) soon became apparent *after* aortography. The nephritic process was not, however, affected adversely by the examination, to judge from the clinical course. Special pre-aortographic findings included inulin clearance 34 ml/min, PAH clearance 221 ml/min, renal

circulation 356 ml/min, and filtration factor 0.15. These tests were repeated about two months after aortography, with the following results: inulin clearance 49, PAH clearance 334, renal circulation 576 and filtration factor 0.15. Case 2 showed a congenital anomaly in the form of a horseshoe kidney lying in the pelvis, and gave a history of recurrent cystopyelitis. This patient also seemed to be unaffected by the investigation. Aortography ought not, perhaps, to have been carried out on these two patients owing to the impaired renal function. The first of these cases, however, exhibited an atypical clinical picture, with unilateral interruption of renal function; and in the second, with a pelvic kidney, the renal outlines could not be exactly defined by urography.

An important question is whether ganglionic block affects renal function. There appears to be nothing to show that this is so.

Among 40 aortographies performed under ganglionic block we have on one occasion encountered temporary impairment of renal function of the lower nephron nephrosis type following the procedure. In this case 40 ml Umbradil 70 % had been injected with a pressure syringe; since then the use of the pressure syringe has been discontinued and the amount of contrast reduced to 30 ml. Renal function improved rapidly, and nephrectomy 4 weeks later, was uncomplicated. Clearance tests 8 months after aortography gave satisfactory results. The follow-up report of 14 cases of acute tubular necrosis (LOWE 1952) indicate that once recovery from the crisis has been made a favourable prognosis can be given.

Grave renal lesions following aortography indeed occur, but in relation to the number of investigations are rare. The risk associated with aortography must be viewed in the light of the risk in surgical exploration of the kidney. Renal damage may arise as follows.

1. Direct trauma may take place due to injection of a large volume of contrast medium under high pressure. The lesions reported have commonly consisted of unilateral damage due to faulty introduction of the needle, the entire volume of contrast medium gushing into the one renal artery. We believe that the use of ganglionic block, intra-aortic catheterization, and smaller volumes of contrast medium under lower pressure result in a lessening of the risk of mechanical injury.

2. Toxic or allergic reaction to the contrast medium may occur. IDBOHRN and BERG (1954) have shown in animal experiments that the non-toxic concentration is exceeded when contrast medium is injected directly into one renal artery. They add that renal angiography repeated at short intervals may cause lesions, despite the use of non-toxic doses on each occasion (see ALWALL et coll.). The lesion in the case described above may probably be attributed to this cause.

The main advantage of ganglionic block in aortography is that the

patient's subjective discomfort becomes insignificant. We believe general anaesthesia to be unnecessary, premedication with morphine and scopolamine followed by a small dose of pethidine before the injection of contrast medium having in our experience proved adequate. During aortography under local anaesthesia alone the patient commonly experiences a burning, cramplike pain at the time of the injection of the contrast medium. This sensation appears to be greatly diminished by the ganglionic block.

As in LINDGREN's procedure, we obtain a good nephrographic effect and it is possible to reduce the volume of contrast medium and pressure of injection. We therefore perform the injection manually. The volume of the contrast medium injected has been cut down from 40 to 30 ml and can probably be diminished even further. In this series we have used the 70 % contrast medium in all but one of the cases in order to test the renal function for this high concentration; there is no doubt however that the concentration can be reduced.

Conclusions

The present investigation has shown no impairment of renal function in 15 cases examined under ganglionic block. Among 40 earlier cases so examined there has been one case of temporary renal failure, probably due to allergic or toxic reaction. The authors' experiences thus show the risks of renal damage in aortography carried out with the technique described to be small. Tests of renal and liver function should precede aortography, which ought not to be carried out in the presence of diffuse parenchymatous lesions.

SUMMARY

An account is given of renal function following aortographies carried out under ganglionic block, the main advantage of the latter being that the aortography may be carried out under local anaesthesia with insignificant discomfort to the patient and with the same results as when the examination is performed with general anaesthesia and hypotension. Tests of renal function have been performed on 15 patients. No signs of renal damage have been noted. One case of temporary renal failure has occurred in an earlier series of aortographies carried out under ganglionic block.

ZUSAMMENFASSUNG

Die Verfasser berichten über die Nierenfunktion nach Aortographien bei Ganglionblockade. Der Hauptvorteil dieser Technik ist die Möglichkeit, die Aortographie in Lokalanästesie bei geringem Unbehagen für die Patienten und mit dem gleichen Resultat wie in Unterdrucknarkose durchführen zu können. Nierenfunktionsproben sind bei 15 Patienten angestellt worden. Keine Anzeichen eines Nierenschadens sind beobachtet worden. In einer früheren Serie von Aortographien bei Ganglionblockade ist in einem Fall eine vorübergehende Nierenschädigung aufgetreten.

RÉSUMÉ

Les auteurs présentent un bilan de la fonction rénale après des aortographies faites sous blocage ganglionnaire dont l'avantage principal est qu'on peut faire l'aortographie sous anesthésie locale avec un désagrément minime pour le malade et en obtenant les mêmes résultats que quand l'examen est fait sous anesthésie générale et hypotension. Des épreuves fonctionnelles rénales ont été pratiquées sur 15 malades. On n'a pas noté de signe de trouble rénal. Il y a eu une insuffisance rénale transitoire dans un cas d'une précédente série d'aortographies faites sous blocage ganglionnaire.

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CHOLEGRAPHY

The new contrast medium Biligrafin

by

Heinz Oeser and *Walter Frommhold*

The history of cholecystography is the history of the contrast media used for visualization of the gall-bladder and biliary passages. Since the pioneer work of GRAHAM and COLE in 1924 (10) every contrast medium used has contained iodine, combined with a hepatotropic vehicle. The chemical and pharmacologic properties of the iodine carrier determine the toxicity, the extent of the side-effects, the form of administration, and the timing of the examination, as well as the general value of the procedure.

In a historical review, four phases in the development of agents for roentgen examination of the gall-bladder and the biliary tract may be distinguished.

During the first phase (1924—1940), sodium tetraiodophenolphthalein was the best-known contrast medium. The commercial preparations had to be injected intravenously, and very often caused extremely unpleasant side-effects (nausea, vomiting, etc.).

The second phase began in 1940 when DOHRN and DIEDRICH (5) introduced β-(4-hydroxy-3, 5-diiodophenyl-)-α-phenylpropionic acid under the name of Biliselectan (Priodax in the U. S. A.) for peroral cholecystography. In numerous commercial preparations this compound is now known throughout the world. Its advantages and characteristics led to the rapid displacement of preparations containing the dangerous phenolphthalein group as iodine carrier, previously used.

The third phase (from 1952) was characterized by the introduction of three iodine atoms into the molecule of the contrast agent. The iodine content rose from about 52 % in Biliselectan to about 66 % in Telepaque, Teridax and Triodan (7—15, 18, 19). The intensity of contrast was thus enhanced in the radiograph, as a result of which non-opaque calculi were better outlined.

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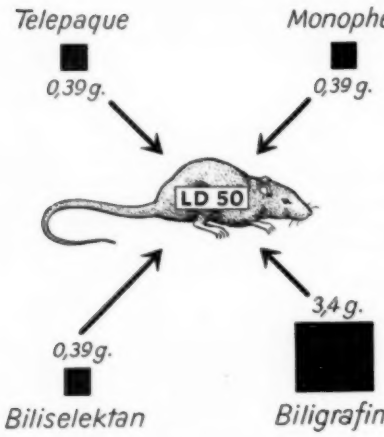


Fig. 1. Toxicity of various biliary contrast media on intravenous injection into animals (LD_{50} in the rat: g per kg body weight).

The fourth phase in the history has now (1953) been entered with the discovery by LANGECKER, HARWART and JUNKMANN (11) of adipic-di-(3-carboxy-2,4,6-triiodoanilide) as a hepatotropic substance. The neutral sodium salt of this substance is readily soluble in water, although on peroral administration it remains almost unabsorbed. One drop of a 40 % solution produces no irritation in the rabbit's eye. In a 20 % solution the substance is practically isotonic with physiologic saline, and is, therefore, admirably suitable for intravenous injection. Signs of local irritation, or fairly severe pain in the veins, do not appear. The toxicity on intravenous administration has been determined in extensive animal experiments (Fig. 1) and amounts to only 1/10th of that of Biliselectan and Telepaque solutions of the same strength.

As with the triiodo compounds, the 64.3 % iodine content of Biligrafin lies considerably above that of Biliselectan. The increase in the opacity with an increase in the thickness of the layer of the medium may be seen from Diagram 1.

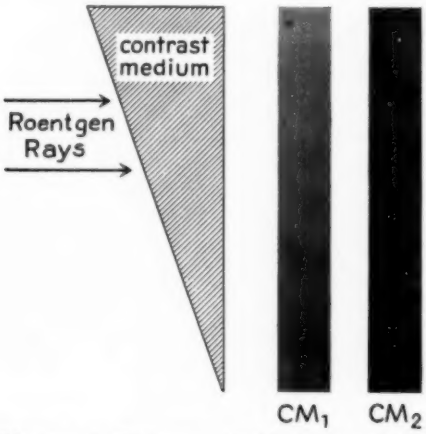
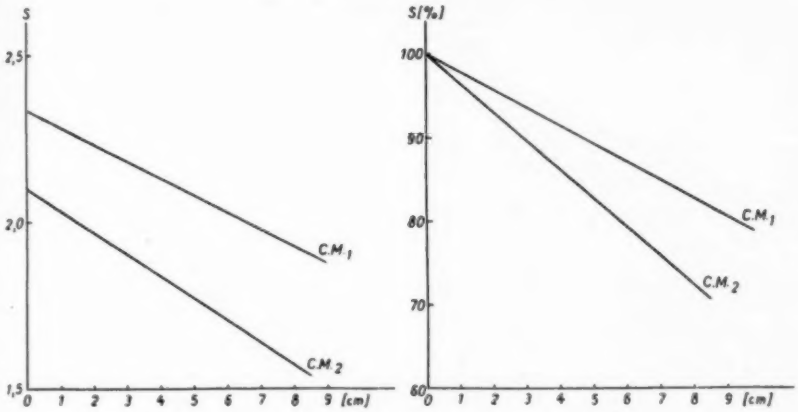


Diagram 1. Differences in blackening of film with layers, increasing wedge-fashion, of Biligrafin (CM 1) and Biliselectan (CM 2).

Uniform layers of 20 % solution of Biligrafin (CM 1) and Biliselectan (CM 2) increasing in thickness in wedge-fashion produce significantly different blackening of a roentgen film, as a result of the differences in absorption of the rays by the contrast agent (Diagram 1). Photometric evaluation of the films shows that not only is absorption greater as a result of the increased content of iodine, but the increase in contrast with increase in thickness of layer is even more marked (Diagram 2 a). If the photometrically determined values ($S = \log \frac{I_0}{I}$) for blackening of the film at the sites of greatest absorption are taken as 100 %, then the increased attenuation of the radiation by



a. b.

Diagram 2 a and b. Photometric evaluation of the differences in blackening in Diagram 1.

Biligrafin, even in thin layers, can be proved (Diagram 2 b). This is the factor determining the increase in contrast with surrounding soft parts and radiolucent calculi.

A critical survey of the second and third phases shows that the limits of clinical efficiency had been reached with the peroral contrast agents mentioned above. Inter alia, this opinion is supported by the results of studies with labelled Biliselectan (I^{131}) (13, 14).

The *peroral administration* of contrast agents appeared at first to represent a great advance in comparison with the intravenously injected and dangerous phenolphthalein preparations. It did not, however, permit any prediction of the extent or speed of absorption and it was quite common to encounter residues in the bowel; these are found less frequently with Biliselectan (although up to 25 %) (2) than, for example, with Telepaque (7, 8, 18, 20). It is true that these residues are an indication that the contrast medium has actually been ingested by the patient; on the other hand, they render the interpretation of the poorly-filled or non-functioning gall-bladder most difficult.

The excretion of contrast agents belonging to the second and third phases is very similar and takes place to a great extent through the kidneys. Only a small proportion is eliminated in the faeces (Fig. 2). Of the total quantity of Biliselectan administered, 60 % to 80 % may be demonstrated in the urine both of animals and human subjects up to 48 hours after administration; only 20 % to 40 % is recovered from the faeces. Diagram 3 gives data on the concentration of the contrast medium in the liver bile in animal experiments. These results correspond closely to those in human subjects. There is also an entero-hepatic circulation of the contrast agent, the extent of which is unknown in individual cases.

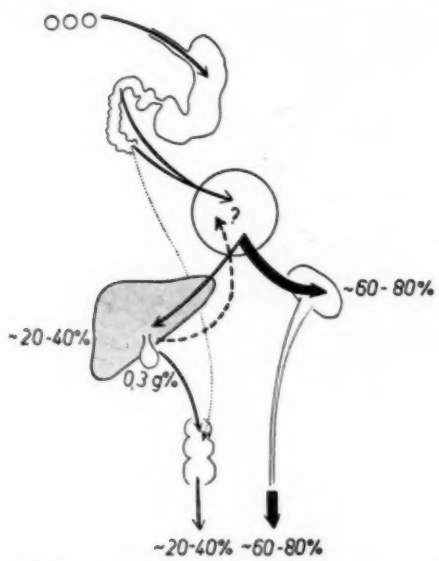


Fig. 2. Excretion mechanism of Biliselectan.

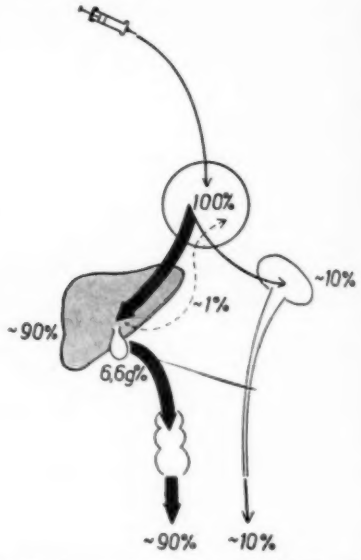


Fig. 3. Excretion mechanism of Biligrafin.

The concentration in the bile is so small that the large extrahepatic biliary passages are only occasionally visualized in special circumstances. It is never possible to show the intrahepatic ducts. Every radiologist is faced with this drawback when the question arises of a calculus overlooked in the biliary passages after cholecystectomy.

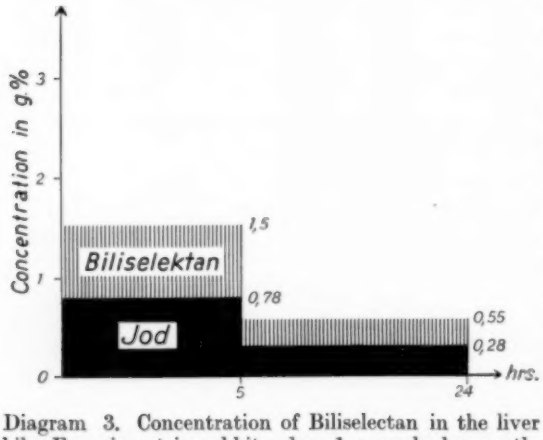


Diagram 3. Concentration of Biliselectan in the liver bile. Experiment in rabbits: dose 1 g per kg by mouth.

The mechanism of excretion of the triiodated contrast agents is essentially similar. Their introduction may therefore be designated only as a partial advance. The filled gall-bladder is probably better visualized in the radiograph. Our further assessment of the situation is, however, more cautious than that of WHITEHOUSE and MARTIN (20), who with other investigators (3, 6, 16), considered Telepaque to be

more reliable than Priodax as regards radiologic visualization of the gall-bladder. We found by careful re-testing that a negative cholecystogram with Biliselectan usually remains negative on repetition with another peroral contrast agent. We are also sceptical about the figures cited in the literature for positive cases, since the composition of the series decisively affects the proportion of successes. This is evident from other series in which a comparison is said to have shown a slight advantage in favour of Priodax as against Telepaque (12, 17).

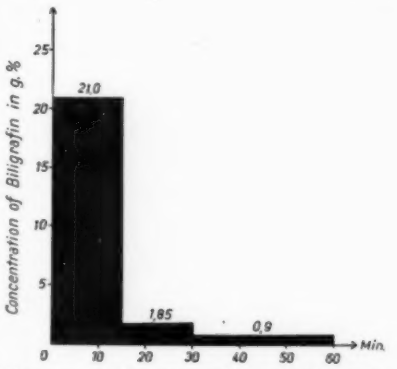


Diagram 4. Concentration of Biligrafin in the liver bile — hepatic duct — during the first hour after intravenous injection. Experiment in rabbits: dose 0.1 g per kg.

The physiologic variation in the urinary excretion of Biliselectan labelled with I^{131} is wide, amounting to 28 % to 82 % of the dose in 48 hours (13). Concentrations in the urine and blood are also subject to great variation. Pathologic conditions or functional peculiarities cannot be differentiated. The cause of failure of the gall-bladder to fill with contrast agent in individual cases could not be elucidated in this manner.

The excretion of adipic-di-(3-carboxy-2,4,6-triiodoanilide) differs basically from that of other known contrast media (Fig. 3). It is characterized by the fact that about 90 % of the substance is excreted via the liver into the bile and the faeces, only about 10 % leaving the body in the urine. The relatively unimportant entero-hepatic circulation may be neglected. The almost selective hepato-tropic carrier is responsible for the hitherto unattainable concentration of the medium in the bile. In experiments in dogs, the level of this substance in the bile was about 30 to 100 times higher than the plasma level. Intravenous injection into rabbits also led to concentrations in the liver bile several times higher than with Biliselectan (Diagram 4). Cook et coll. (4) interpret this as a sign of active excretion of the substance through the liver cells. This totally different mechanism of elimination, which determines the superiority of this contrast agent, has been confirmed in investigations on patients.

Case 1. 48-year-old man. Operation for occlusion of the common bile duct by a calculus following cholecystectomy 2 years previously. After operative exposure of the common bile duct, the contrast medium (40 ml Biligrafin 20 %) was injected intravenously at the moment when the surgeon incised the duct to remove the calculus. By means of the insertion of a T-drain, bile was collected in individual portions beginning 5 minutes after the injection. Up to 40 minutes after the injection the branch of the tube leading

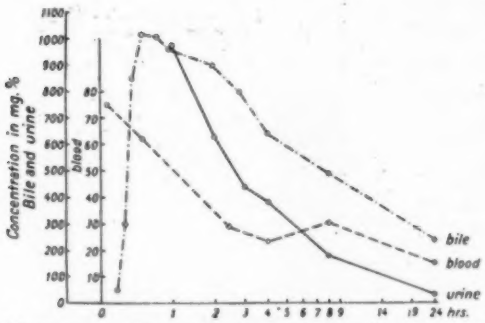


Diagram 5. Concentration of Biligrafin (Case 2). Following cholecystectomy: occluding stone at the papilla of Vater. See also Fig. 6 a and b.

to the duodenum was closed with a clamp, so as to ensure that all the bile secreted was collected for examination. The same effect was obtained by suction drainage after the termination of the operation. The picture was completed by urine analysis and determination of the bile level in the blood.

The concentration curves in Diagram 5 show the remarkably high content of contrast medium in the bile during the first two hours after injection, the figure then falling relatively rapidly. The total balance (Diagram 6) reveals the significant difference from earlier contrast agents. Within 24 hours of the injection, 59.8 % of the total dose was excreted in the bile. During the same period, only 19 % was found in the urine. If it be remembered that a small portion of the bile gets through to the duodenum in spite of the suction drainage — the stools were never bile-free — it is clear that at least 75 % to 80 % was excreted in the bile.

These astonishing values have been confirmed by studies with labelled Biligrafin. Of the dose, 70 % was found in the faeces within 48 hours of injection, and only 10 % to 13 % in the urine (1).

We have found studies in patients with biliary fistulae particularly valuable. If measurements on faeces and urine during Telepaque cholecystography have given similar end-values for excretion products, then, in our opinion, these should not be related to the mechanism of elimination until similar methods of measurement have disproved that the high Telepaque content of the faeces is to a large extent due to unabsorbed residues of the contrast agent.

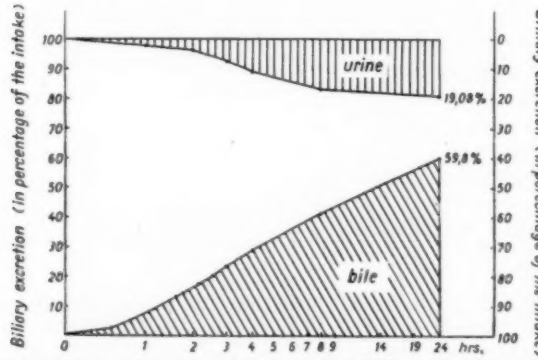
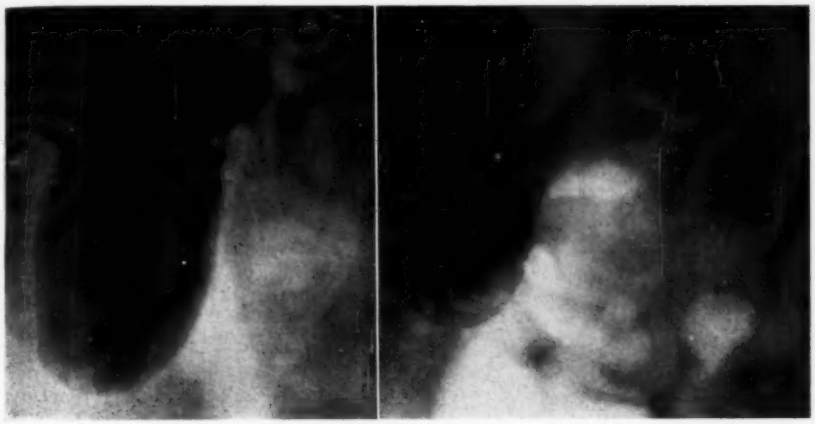


Diagram 6. Excretion after use of Biligrafin (Case 2). See also Diagram 5.

In our Department we are now able to survey nearly 1,000 Biligrafin cholegraphies. Since



a. b.

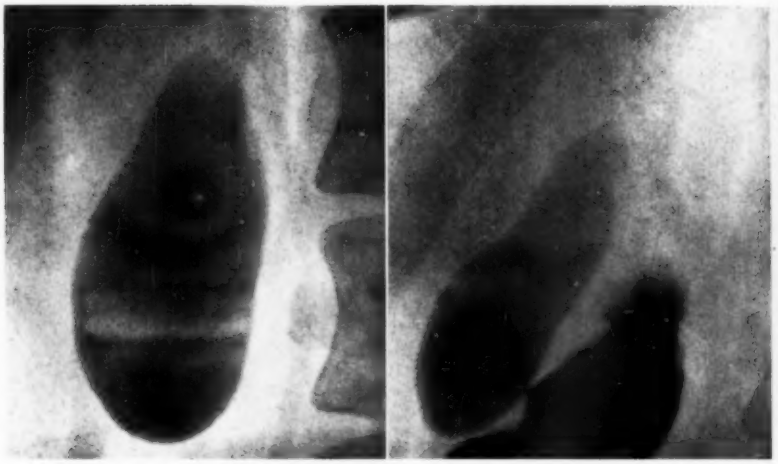
Fig. 4. Normal cholegraphy with Biligrafin. a. Radiograph 2 hours after injection of 20 ml Biligrafin. b. Radiograph 30 min. after egg-yolk meal. Visualization of large extrahepatic biliary passages.

we were the first to work with the substance, we feel justified in also referring to all the experience gathered elsewhere, even outside Germany.

A normal dose of Biligrafin (produced by Schering A. G. Berlin West) amounts to 20 ml of a colourless 20 % solution, or 4 g of the active agent. For the study of specific problems, especially the investigation of cholecystectomized patients, we have recently used 20 ml of a 40 % solution still under clinical trial. It was as well tolerated as the normal solution. We consider it preferable, especially as regards injection technique, to employ Biligrafin 40 % rather than to inject the double dose (40 ml = 2 ampoules) of Biligrafin 20 %, as recommended by many German authors (9).

The technique of examination does not differ essentially from that commonly employed.

In routine examinations, the optimum concentration of the contrast medium in the gall-bladder is reached about 2 hours after injection. In the great majority of cases, the large extrahepatic ducts are still recognizable at this time. After a suitable meal to ensure stimulation of the gall-bladder, for which we like to use two egg-yolks, an assessment of the functional state of the gall-bladder is possible (Fig. 4 a and b). It is, however, not uncommon to find layer formation of the contrast agent in the gall-bladder in films obtained with the patient erect. Narrow light stripes may simulate a row of small floating calculi. This appearance



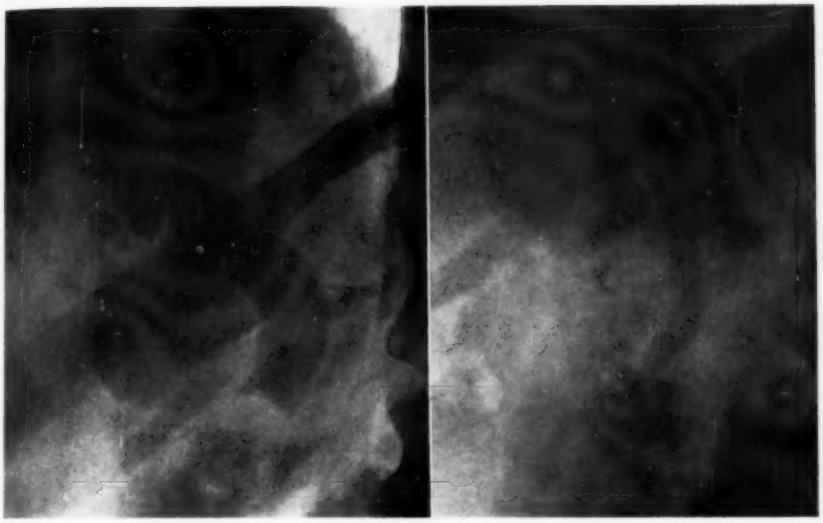
a. b.

Fig. 5. Normal cholegraphy. a. Layer formation of contrast agent: patient erect 2 hours after injection of 20 ml Biligrafin. b. 30 min. after egg-yolk and barium meal. Good gall-bladder function. Disappearance of layer appearance.

depends on the difference in the specific gravity between the bile and the inflowing highly concentrated Biligrafin. In no circumstances should this layer formation be interpreted as a pathologic sign. It disappears on contraction of the gall-bladder, *e. g.* after a meal of egg-yolk which acts as a stimulator (Fig. 5 a and b), and is naturally never seen if radiographs are taken with the patient lying down.

For visualization of the biliary passages we recommend that radiographs be taken with the patient prone on the Bucky table. Corresponding to the rapid and highly concentrated excretion, the ribbon-like shadows of the larger biliary ducts may be differentiated as early as 10 minutes after the injection of 20 ml of Biligrafin 40 % or 40 ml of Biligrafin 20 %. The relationship of the biliary ducts to the vertebral column enables the positioning to be adjusted before taking the serial radiographs which should now follow at 10 minute intervals. It is usually best, and often indeed necessary, to turn the patient into the second oblique position. Optimum visualization, even of the intrahepatic ducts, is obtained between 40 and 90 minutes after injection. A definite opinion upon the function of biliary flow after cholecystectomy thus becomes a matter of routine.

Calculi occluding the common bile duct but not radio-opaque, the presence of which was previously never diagnosed, are now revealed by



a. b.

Fig. 6. Case 2. Cholegraphy. a. Radiograph 80 min. after injection of 20 ml Biligrafin 40 %. Visualization of an occluding stone at the papilla of Vater. Stasis in the biliary tract. b. Radiograph 40 min. after the injection of 20 ml Biligrafin 40 %. Three months after removal of occluding stone: return to normal of bile flow.

the appearance of dilated biliary passages with stasis and a sharp delimitation of the contrast shadow, convex cranially.

Case 2. 48-year-old woman. Cholecystectomy 2 years previously, since when repeated colic; several weeks in hospital for conservative treatment because calculi were not demonstrable. Cholegraphy with Biligrafin (Fig. 6 a) distinctly shows a stone the size of a plum-stone, occluding the papilla of Vater; this has led to an extraordinary degree of stasis as far as the liver. Operation confirmed the finding and the calculus was removed. Three months later the patient was completely free from symptoms. A control radiograph showed return to normal of the previously dilated biliary passages (Fig. 6 b).

Even when the biliary tract is not completely occluded, calculi giving rise to severe colic may be discovered.

Case 3. 32-year-old woman. Biliary symptoms since 1942. Peroral cholecystography in 1947 showed no signs of calculi. Gallstones were demonstrated in 1949; cholecystectomy performed in 1951. Symptom-free until June 1953, when increasing colic, nausea, but no jaundice. Examinations with Biliselectan and Telepaque gave no visualization of the biliary tract. Cholegraphy with 20 ml Biligrafin 40 % revealed multiple calculi in the common bile duct (Fig. 7).

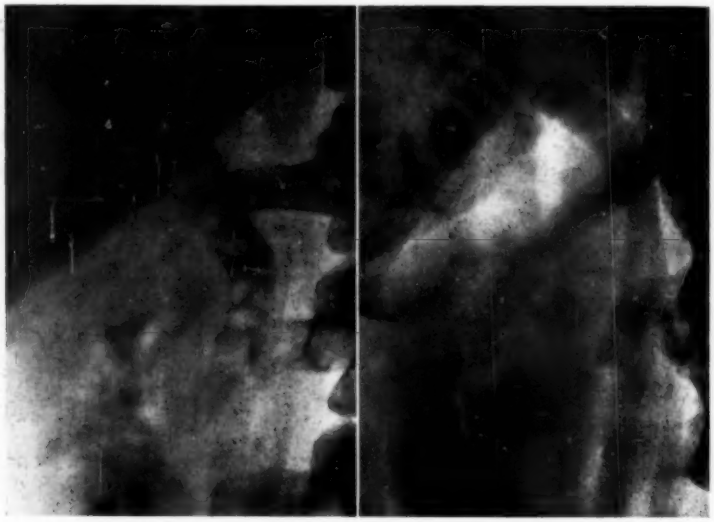


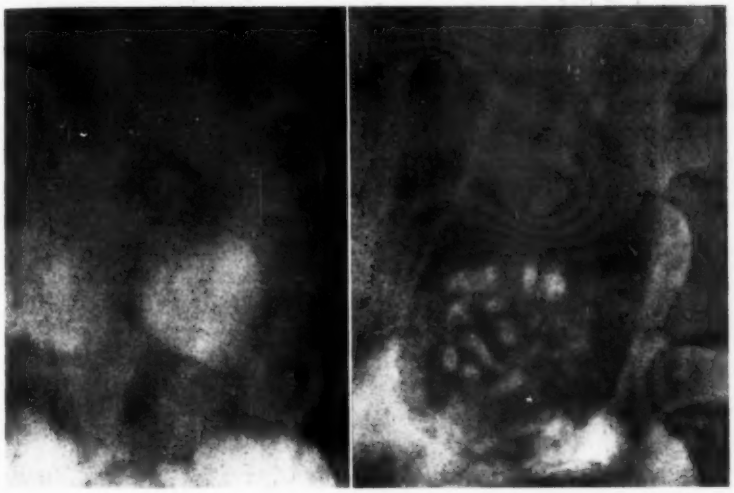
Fig. 7. Fig. 8.

Fig. 7. Case 3. Cholegraphy. Radiograph 20 min. after injection of 20 ml Biligrafin 40 %. Visualization of multiple calculi in the common bile duct.

Fig. 8. Cholegraphy. Radiograph 90 min. after injection of 20 ml Biligrafin 40 %. Visualization of dilated common bile duct. Probable occluding stone at papilla of Vater; gall-bladder not seen. (Occluding stone confirmed at operation. Gall-bladder and cystic duct filled with numerous calculi.) Delineation of duodenal loop with regular mucosal pattern.

Excretion of the contrast medium from the gall-bladder into the small intestine takes place in such high concentrations that shadows with adequate contrast are always observed in the duodenal loop in films obtained 30 to 90 minutes after the injection. The circular folds in the mucosa are usually very distinctly visualized. The form and size of the C-loop may be assessed (Fig. 8) and it should doubtless be possible to detect by this means deformities due to periduodenitic adhesions or displacements of the duodenum due to tumour.

Further investigation is necessary to determine whether Biligrafin may also be used as a means of estimating liver function. The fact that this is not possible with Biliselectan (13) does not permit the conclusion that no insight into the complicated processes of the hepato-biliary system may also be obtained with Biligrafin. Investigations are in progress with Biligrafin in which the iodine atoms have been tagged with I^{131}. These should bring further enlightenment. In experiments in rabbits, it has



a. b.

Fig. 9. a. Telepaque cholecystography: gall-bladder not visualized. b. Cholegraphy with Biligrafin 40 %: gall-bladder outlined and seen to be full of calculi.

been found that the figure of about 10 % for renal excretion rises considerably if there are disturbances in the hepato-biliary system. This might form the basis for a liver function test. It will, however, be necessary to relate results of serum protein electrophoresis to these studies, since 80 % of the contrast substance is bound to the plasma protein as transport medium. A non-filling of the gall-bladder is not necessarily due to a disturbance in the liver-bile system. The possibility of a pathologic composition or disturbance in the formation of the blood proteins must be taken into consideration in every case.

Side-effects, which used to be so much feared when intravenous cholecystography was practised with preparations of the phenolphthalein group, are practically non-existent with Biligrafin. They are decisively influenced by the injection technique. With any contrast agent containing iodine, trivial side-effects will be observed in about 5 % to 20 % of patients. They are not to be considered as indicating hypersensitivity to iodine but rather to the whole molecule of the contrast substance, and consist, as in urography, of mild nausea and, rarely, of vomiting. It should be recalled that Biligrafin lowers the blood pressure. The injection must therefore be given particularly slowly to hypotensive patients and those with a labile circulation. In general, 5 to 6 minutes is sufficient for the injection, which should be guided by the patient's condition. If the in-

jection is given more rapidly, unpleasant sensations varying from a feeling of heat to severe vomiting must be expected. On the other hand, we have never encountered noteworthy reactions in the gastro-intestinal tract or diarrhoea. Both these are relatively common when Biliselectan is employed. According to a communication from Schering A. G., Biligrafin has never caused a fatal outcome in about 40,000 examinations.

It is customary to assess the value of a contrast agent by the percentage of positive cases of visualization of the gall-bladder attained. We adopt a cautious attitude to this view, since such statistics, as already emphasized, depend essentially on the composition of the series. For this reason, we are not presenting a statistical evaluation of our examinations with Biligrafin. We have, however, on several occasions made the observation that in cases in which no visualization of the gall-bladder was possible with Biliselectan and Telepaque an examination with Biligrafin 40 % revealed gallstones, the presence of which was suspected on clinical grounds (Fig. 9 a and b). In our opinion, this and other observations offer more convincing proof of the superiority of the new contrast substance than statistical figures.

The purely technical advantages of intravenous cholegraphy over the peroral method are obvious. In studies on ambulant patients or in cases of medico-legal importance, intravenous injection of Biligrafin is the method of choice, since this does away with the uncertainty whether the patient has in fact taken the tablets or granules the previous evening. The shortening of the examination time from 15 hours with Biliselectan to 2 hours with Biligrafin increases the certainty of finding the optimum state of filling of the gall-bladder, and in itself should constitute an advantage.

We would stress that the introduction of Biligrafin, with its basically different chemical structure and completely new type of excretion mechanism, does not represent merely a further development of substances previously used in cholecystography but augurs an entirely new chapter in the radiologic diagnosis of diseases of the biliary tract.

SUMMARY

Cholecystography and the contrast agents employed are surveyed. The introduction of Biligrafin does not represent a simple development of the triiodated contrast agents but opens a new chapter in the radiologic diagnosis of diseases of the biliary tract. The time of examination is considerably shortened and side-effects are almost absent; the high concentration of the medium permits reliable visualization of the biliary tract even when cholecystectomy has been performed. The suggestion is made that Biligrafin may be found to be of value in the estimation of liver function.

ZUSAMMENFASSUNG

Historischer und kritischer Überblick über die Cholecystographie und ihre Kontrastmittel. Die Einführung des Biligrafin stellt keine einfache Weiterentwicklung der trijodierten Kontrastmittel dar, sondern leitet einen neuen Abschnitt in der röntgenologischen Diagnostik von Erkrankungen der Gallenblase und Gallenwege ein. Die Untersuchungsdauer wird erheblich abgekürzt und Nebenwirkungen fallen nahezu völlig weg; die hohe Konzentration des Mittels erlaubt eine einwandfreie Darstellung der Gallenwege auch bei cholecystektomierten Patienten. Es wird angedeutet, dass Biligrafin wahrscheinlich für die Beurteilung der Leberfunktion von Wert werden kann.

RÉSUMÉ

Les auteurs font une revue de la cholécystographie et des produits de contraste. L'introduction de la Biligrafin ne représente pas seulement un perfectionnement des produits de contraste tri-iodés mais elle ouvre un nouveau chapitre dans le diagnostic radiologique des affections des voies biliaires. La durée de l'examen est considérablement diminuée et les incidents sont presque absents; la forte concentration du produit de contraste permet une visualisation exacte des voies biliaires, même quand on a fait une cholécystectomie. Les auteurs suggèrent que la Biligrafin pourrait se montrer utile dans l'examen de la fonction hépatique.

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SIDE-EFFECTS OF BILIGRAFIN

by

Georg Theander

Since the introduction of cholegraphy with Biligrafin, an iodized contrast medium for intravenous use (FROMMHOLD 1953), the method has been employed with increasing frequency and is now a routine procedure at many hospitals. As the method is of such recent date, reports of any side-effects of the contrast medium must presumably be desirable. The present paper is concerned with an analysis of such untoward reactions.

Earlier Reports

Judging by animal experiments, the toxicity of Biligrafin is low. LANGECKER, HARWART & JUNKMANN (1953) found the LD 50 for rats to be 3.4 g/kg body weight, and histologic examination of the liver and kidneys of rats killed 2 to 9 days after the intravenous administration of Biligrafin in a dose of 1 g/kg body weight showed no pathologic changes. In the cat, a slight reduction of blood pressure was observed after the intravenous administration of a dose of 0.2 g/kg body weight.

Cumulative clinical evidence also suggests that Biligrafin is only slightly toxic. FROMMHOLD (1953) observed vomiting as the only side-effect, and then in only 1 of 300 cases. GAEBEL & TESCHENDORF (1953) also reported nausea and vomiting as the only side-effects of Biligrafin. NISSEN & HORSTMANNSHOFF (1953) described nausea on one occasion and shivering on another. Of PÜSCHEL's (1953) cases, vomiting occurred in 1, shivering in 1, and a fall in the blood pressure to 25 mm Hg in 1. Sensation of warmth or upper abdominal pressure, vomiting, perspiration, shivering and circulatory collapse were noted in some of the 80 cases reported by HUBER & STÖSSEL (1954), but, according to them, no alarming complications occurred. A sensation of warmth, dizziness and nausea were the only side-effects described by PAHL (1954). He also carried out clinical liver function tests after cholegraphy and the values recorded were within a normal range throughout. SCHILLING (1954), with a series of 140 examina-

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tions, reported untoward reactions on 12 occasions: tachycardia and nausea on 4, upper abdominal pressure on 3, headache on 2, a sensation of warmth on 1 and brief circulatory collapse on 2. PUHLMANN (1954) reported nausea or a sensation of warmth in 4 per cent of almost 200 examinations. On only 1 occasion was vomiting noted.

CAROLI et coll. (1954) observed no noteworthy side-effects in their series of more than 100 examinations. NADAL & VIGNEAU (1954) noted pruritus and a sensation of warmth in 1 of their 14 cases; SÉNÈQUE et coll. (1954) reported swooning as the only side-effect of Biligrafin on 1 out of 60 occasions. ARIANOFF (1953) recorded nausea on 3 occasions and itching on 4 in a series of 37 cases. VAN DOORN (1954) reported urticaria on 1 occasion and a sensation of warmth or nausea in some of his 113 cases.

Of 103 patients examined by RUCKENSTEINER (1954), 4 complained of nausea, several of a sensation of warmth and 1 of a disagreeable taste in the mouth. Slight nausea, dizziness, sneezing or restlessness was noted by ORLOFF et coll. (1954) in a few of their 30 cases, and BERK et coll. (1954) recorded perspiration and erythematous patches on the face or a burning sensation in the eyes, nose and face in 3 out of 30 cases.

In cholegraphy in children, 12 days to 3 years old, no side-effects were seen during or after examination with Biligrafin in a dose of 0.1—0.4 g/kg body weight (THEANDER 1954); no histologic changes attributable to Biligrafin were seen in the 2 cases of this series in which autopsy was performed about a month after the roentgen examination.

Severe untoward reactions to Biligrafin are, however, on record. Thus, HAGEDORN (1953) reported severe circulatory collapse in 2 of 50 patients. In a material consisting of 274 examinations, HORNYKIEWYTSCH & STENDER (1953) observed exacerbation of the cholangitic process and signs of increasing liver damage in 2 cases of paratyphoid cholangitis. In 2 cases of tetany, the administration of Biligrafin was followed by convulsions. Slight reactions occurred in 6 per cent of the entire material.

Unless otherwise stated, Biligrafin was given in a dose of 4 g or 8 g in the investigations referred to above.

Material

The present material consisted of the first 500 cholegraphic examinations performed at the Roentgen Department of Malmö Allmänna Sjukhus. Biligrafin was used in 20 per cent concentration in 431 of these examinations. In a number of unselected cases (69 examinations), a 40 per cent preparation was employed. (The Biligrafin in a 20 per cent solution is the commercially available disodium salt of N:N'-adipin-di-(3-amino-2:4:6-triiodobenzoic acid). The 40 per cent preparation is a lithium salt of the same substance, supplied by the courtesy of Schering

A. G., Berlin.) In 229 examinations, the dose of the contrast medium was 12 g, in 271 it was 8 g or less. For children, the dose was reduced according to body weight.

The contrast medium was injected slowly (about 5 to 10 minutes). On the appearance of side-effects, if any, the injection was interrupted. In a few cases in which there was reason to assume hypersensitivity, the patients received a test dose of 1 ml of Biligrafin 20 %, intravenously, but none of these test doses produced any signs of hypersensitivity.

The examinations were carried out on 437 patients, ranging in age from 12 days to 85 years (138 males and 299 females). Of these patients, 42 were examined twice, 7 three times, 1 four times and 1 five times. The interval between any two consecutive examinations of a patient was at least 2 days. On 67 occasions, the examination was performed in the presence of jaundice, apparent from the discoloration of the sclerae or revealed by laboratory tests (hyperbilirubinemia). On 347 occasions, jaundice was not present. As to the remaining 86 examinations, it is not known whether they were performed in the presence or absence of jaundice.

Side-Effects

Slight general discomfort, dizziness, flushing, perspiration and nausea of short duration, which were fairly common, were not taken into account in the present investigation. Other signs and symptoms occurring during or after cholegraphy were regarded as side-effects of Biligrafin unless some other more plausible explanation was available. All reactions regarded as due to hypersensitivity were noted, no matter how trivial they appeared to be.

No attempt was made routinely to analyse the influence of Biligrafin on the functional capacity of the excretory organs, *i. e.* liver and kidneys. Only in 46 patients was the serum bilirubin determined 7 days, at the most, before and 7 days, at the most, after cholegraphy. In 16 of these, the serum bilirubin was normal (1 mg per 100 ml or less) before cholegraphy; afterwards it was pathologically increased in 4 of these cases, this increase being reasonably due to an operation on the gallbladder performed in the meantime. In 30 of these 46 patients, the serum bilirubin was increased before cholegraphy. After cholegraphy, the increase persisted unchanged in 1, was smaller in 22, and greater in 7. One of these 7 patients had, in the meantime, been operated on. In view of the wide transient fluctuation often occurring in such patients, it is debatable whether an increase in the serum bilirubin can be attributed to Biligrafin in any of the cases thus tested.

Untoward reactions appearing during or soon after the examination, *i. e.* before the patient left the Roentgen Department (usually about 1 to 4 hours), were classed as early, the remainder as late. As to late reactions, information was usually obtained from the patients within 2 to 3 days. The record sheets of some patients are, however, incomplete in this respect; this should be borne in mind in the evaluation of the statistical analysis of late reactions.

Incidence. Early side-effects were noted on 25 occasions (5 per cent): biliary colic on 4, profuse vomiting on 3, signs of circulatory collapse on 3, lacrimation on 2, coryza and sneezing on 3, edema of the face on 2, diarrhoea on 1, and urticaria on 8 occasions; in 1 patient with angina pectoris, in 1 with bronchial asthma and in 2 with epilepsy, the injection of Biligrafin was followed by an acute attack of the respective disease. On some occasions, 2 or more of these untoward reactions occurred in combination.

In 1 of the 8 cases in which urticaria occurred during the examination, allergy had been suspected, but the test dose of Biligrafin had not been followed by any side-reactions.

Late side-effects were seen on 14 occasions (2.8 per cent): protracted nausea with vomiting on 10, biliary colic on 2, diarrhoea on 1 and a severe complex reaction on 1 occasion.

Case extract (Case 318). The patient was a woman aged 41, who presented herself on 3 March 1954 for routine follow-up examination after cholecystectomy, to which she had been submitted 2 years earlier. She denied postoperative symptoms. The serum bilirubin (van den Bergh's reaction) was 1.0 mg/100 ml and the thymol reaction normal (0.09 units). Cholegraphy, 12 days later, revealed no signs of a pathologic condition and no early side-effects of Biligrafin were noted. In the evening, however, biliary colic, headache, hoarseness, vomiting and diarrhoea occurred and the tongue began to swell. With the abatement of these symptoms on the following day, jaundice appeared. The serum bilirubin on 18 March was 3.35 mg/100 ml, on 27 April, 1.2 mg/100 ml and on 21 June, 1.4 mg/100 ml. The erythrocyte sedimentation rate, which was 8 mm/1 hour (Westergren's method) on 3 March, reached 31 mm/1 hour on 18 March and did not return to normal until about 6 weeks later. The thymol reaction increased from 0.09 to 0.34 units; on 21 June it had decreased to 0.23 units.

The patient felt tired and weak for about 3 months after the cholegraphy.

Age and Sex Distribution. It is apparent from Table 1 that age had no definite bearing on the frequency of the side-reactions. Of the 500 examinations, 160 were carried out on males and 340 on females. In the male group, early side-effects occurred on 10 occasions and late untoward reactions on at least 2. The corresponding figures for the female group were 15 and 12. The sexes did not differ statistically as regards frequency of side-reactions.

Table 1

Distribution of side-reactions among age classes

Age in years	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	Total
Number of examinations	13	5	38	96	113	114	81	38	2	500
Number of early reactions	0	0	3	7	8	3	2	2	0	25
Number of late reactions	0	0	0	3	4	4	3	0	0	14

Sensitization. It was thought that, just as certain drugs are capable of producing allergy, Biligrafin might induce hypersensitization to the preparation. If so, side-reactions might be expected to occur more frequently in patients who had been examined with Biligrafin on some earlier occasion. On 437 occasions, the cholegraphic examination was carried out on patients who had never before received Biligrafin. Of these, early side-reactions occurred on 23 and late side-effects on at least 13. In the remaining 63 examinations, performed on patients who had received Biligrafin at least once before, early side-reactions appeared on 2 occasions and late side-reactions on at least 1. No statistical difference was demonstrable between the frequency of the reactions in these two series. Moreover, of those patients who showed side-reactions to Biligrafin at the first examination, 3 were examined again and then none showed any untoward reaction. Observations made in the present investigation did not, therefore, suggest that Biligrafin is capable of producing hypersensitization to the preparation.

Influence of Jaundice. Being normally eliminated mainly (90 per cent) via the liver (FROMMHOLD 1953), Biligrafin must reasonably be less rapidly detoxified in the presence of hepatobiliary insufficiency. Even if the renal elimination of the contrast medium is compensatorily increased (FROMMHOLD 1953), the substance must persist longer in the circulation or in a higher concentration in patients with impaired excretory capacity of the liver. One might therefore be tempted to expect that the presence of hepatogenous or obstructive jaundice, *i. e.* signs of severe hepatobiliary insufficiency, might increase the risk of any side-effects of Biligrafin. None of the 67 examinations performed in the presence of jaundice were, however, accompanied or followed by untoward reactions. Moreover, the difference in the frequency of side-effects between jaundiced and nonjaundiced patients was statistically significant (Table 2). If only those examinations be taken into account in which the sodium salt of Biligrafin was used, the corresponding difference was also significant (Table 3).

Table 2

Relation between the frequency of side-effects of Biligrafin and jaundice. Total material

	Number of examinations	Number of side-reactions	
		Early	Late
Jaundice	67	0	0
No jaundice	347	17	12
Unknown	86	8	2
Total	500	25	14

It thus appears that jaundice protects the patient from undesired effects of Biligrafin, an assumption in good agreement with the effect

of intervening jaundice on certain pathologic conditions. Jaundice has been reported as exerting a favourable effect on rheumatoid arthritis (STILL 1897; HENCH 1933, 1938, 1940, 1950; and others), on bronchial asthma (BOROS 1937; GORIN 1949; KADLUBOWSKI 1950; TURIAF & BLANCHON 1953), on hay fever (BOROS 1937), on migraine (MORLOCK & ALVAREZ 1940) and in hypersensitivity to eggs (HENCH 1940).

The absence of untoward reactions to Biligrafin in the presence of jaundice in the present series is in line with the clinical observations described above, and provides further support for the assumption that jaundice exerts an anti-allergic effect.

The Choice of Preparation. No side-reactions were seen on the 69 occasions the lithium salt of Biligrafin (40 %) was used. Of the 431 examinations with the sodium salt (20 %), 25 were attended by early reactions and at least 14 were followed by late reactions (Table 3).

Table 3

Relation between the frequency of side-reactions and jaundice in examinations performed with the sodium salt of Biligrafin

	Number of examinations	Number of side-reactions	
		Early	Late
Jaundice	57	0	0
No jaundice	290	17	12
Unknown	84	8	2
Total	431	25	14

If only those examinations performed in the absence of jaundice be taken into account, the lithium salt was used on 57 occasions and the sodium salt on 290. Of these 290 examinations, 17 were attended by early side-reactions and at least 12 were followed by late untoward reactions (Table 3). Thus, judging by observations made in the present series the lithium salt is less toxic than the sodium salt.

Influence of Size of Dose. Of the 290 examinations performed with the sodium salt in the absence of jaundice, a dose of 8 g or less was used in 160, and 12 g in 130. The use of the smaller dose was accompanied or followed by early reactions on 7 occasions and by late side-reactions on at least 3; the corresponding figures for the larger dose were 10 and 9.

As to *early* reactions, it should be noted that, when they appeared during the actual injection of the contrast medium, the injection was interrupted. This implies a certain selection with consequent over-representation of the examinations with early side-reactions in the group of patients that received the lower dose. Judging by the distribution of the *late* side-reactions, it is statistically probable that the larger dose produced reactions more frequently than the smaller one.

SUMMARY

The side-reactions observed in connection with 500 consecutive cholegraphic examinations with Biligrafin are described and statistically analysed. They occurred in 7.8 % of cases. The patients tolerated the lithium salt of Biligrafin (40 per cent concentration) better than the sodium salt (20 per cent concentration).

ZUSAMMENFASSUNG

Die Nebenwirkungen, die in 500 aufeinander folgenden cholangiographischen Untersuchungen mit Biligrafin beobachtet wurden, werden beschrieben und statistisch analysiert. Sie traten in 7.8 % der Fälle auf. Die Patienten vertrugen das Lithiumsalz des Biligrafin (Konzentration 40 %) besser als das Natriumsalz (Konzentration 20 %).

RÉSUMÉ

L'auteur décrit et analyse statistiquement les incidents observés à l'occasion de 500 biligraphies consécutives avec la Biligrafin. Ils se sont produits dans 7.8 % des cas. Les malades ont mieux toléré le sel de lithium de la Biligrafin (concentration 40 pour cent) que le sel de sodium (concentration 20 pour cent).

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PERCUTANEOUS LIENO-PORTAL VENOGRAPHY

by

I. Bergstrand and *C.-A. Ekman*

The development of the porta-caval shunt for decreasing the pressure in portal hypertension with hemorrhage from the upper digestive tract has created a desire for preoperative information on the condition of the portal vein and the splenic vein. Two types of operation which have found wide use are the establishment of an anastomosis between the portal vein and the inferior cava or between the splenic vein and the left renal vein. Portal phlebography will help the surgeon to decide which type of operation should be performed in a given case.

In 1945, BLAKEMORE, LORD and WHIPPLE injected Diodrast 35 % into a branch of the portal vein during operation in order to ascertain the site of a portal block. This method, the injection of the contrast medium through a catheter introduced into one of the branches of the portal system at operation, has since been modified and elaborated by several investigators. DE SOUSA PEREIRA (1951) and DUBOST et coll. (1951) directed attention mainly to the extrahepatic portal branches, while MOORE & BRIDENBAUGH (1950) and DANIEL et coll. (1952) focused their interest on the intrahepatic portal branches.

This method requires laparotomy and thus cannot give the surgeon the desired information beforehand. In an experimental study in dogs, ABEATICI & CAMPI (1951) showed that percutaneous injection of contrast medium into the spleen gave a rapid filling of the splenic and portal veins and with sufficient concentration to permit demonstration of their anatomy. LEGER (1951) and BOULVIN et coll. (1951) were apparently the first to describe the clinical application of this method. Since

Roentgen examinations of the portal vein, after percutaneous injection of a contrast medium in the spleen, are often described under various names. In the editor's opinion, the terms used in this paper as well as in the paper by GVOZDANOVIĆ and HAUPTMANN in the March issue, precisely define the method employed. For the sake of uniformity this journal will therefore adopt this terminology in the future. (Ed.)

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then it has been employed and reported on by many (DREYER & BUDTZ-OLSEN 1952; COOPER et coll. 1953; GVOZDANOVIĆ et coll. 1953; MILNES WALKER et coll. 1953; DOGLIOTTI, ABEATICI & CAMPI 1954; HALLENBECK & BRUWER 1954). All these investigators performed the method mainly for obtaining information on the portal system of patients with portal hypertension.

Material

Our material consists of 24 patients (13 males and 11 females), aged from 10 to 78. One of the patients was examined 3 times and 5 were examined twice. Percutaneous lieno-portal venography was thus carried out on altogether 31 occasions. On 10 occasions the examination was performed because of portal hypertension with splenomegaly, and on 6 for checking the function of the porta-caval anastomosis. On 13 occasions, the purpose of the examination was to gather information concerning the intrahepatic portal branches in patients in whom a liver tumour had been assumed. In 10 of these 13 cases, the spleen was found to be of normal size. On the remaining 2 occasions, the examination was carried out in order to obtain a conception of the normal roentgen anatomy of the portal branches. These 2 examinations were performed in the Department of Surgery on two patients about to undergo splenectomy because of blood disease.

Laparotomy was performed following 18 out of 31 examinations; the splenic bed was examined and biopsy specimens were taken. At none of these laparotomies, which were performed 1 hour to 23 days after percutaneous lieno-portal venography, were any signs of splenic hemorrhage detected.

Technique

Of the 31 examinations, 5 were performed during operation in the Department of Surgery; the remaining 26 were carried out in the Roentgen Diagnostic Department, where the following technique was applied.

The bowel was cleared thoroughly and the patient examined in the fasting state. He was premedicated with morphine and scopolamine.

The patient was tested for hypersensitivity to the contrast medium by the intravenous injection of 1 ml of Diodonum 35 %. From wide experience of various kinds of examinations in which intravascular contrast media are employed, it appears hardly necessary to observe the strict precautions in hypersensitivity tests suggested by BOULVIN et coll. (1951). Only in one case was the reaction of the patient such as to contra-indicate the examination. He was a man, aged 60, who had had asthma for 30 years.

The position of the spleen relative to the intercostal spaces varies according to body build and type of inspiration. In contra-distinction to the recommendations of most other workers in this field, we therefore did not always place the puncture in a given intercostal space, but, by means of fluoroscopy and the use of indicators, marked the position of the spleen at maximum inspiration.

Before puncture, preliminary films were taken in order to show the size and shape of the spleen and to determine fairly precisely where, in what direction, and how deep, the needle should be introduced.

An automatic cassette exchanger on which the patient was placed in the supine position, was employed. We use a 10 cm long puncture needle with an outer diameter of 1.5 mm. This needle permits a fairly rapid manual injection. By means of an adjustable collar the needle may be adjusted for insertion to the depth desired. Experience

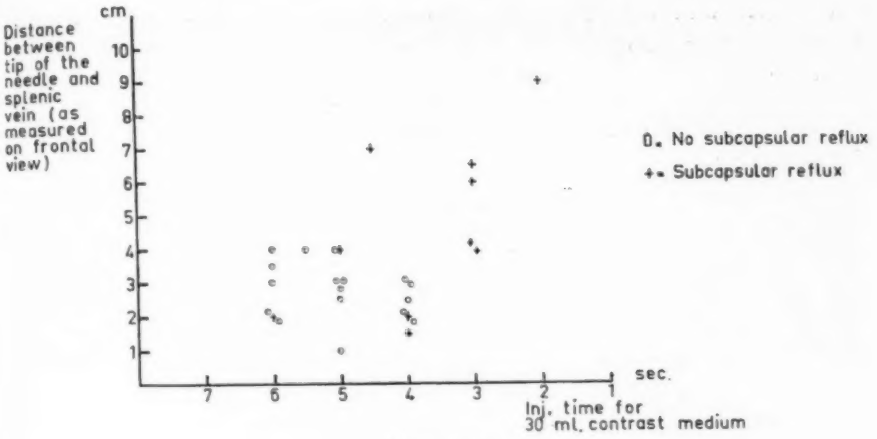


Diagram 1.

has taught us that the closer the tip of the needle is to the hilum of the spleen and the further it is from the site of the puncture in the capsule, the better are the results. In the present series, the needle was inserted 6 to 8.5 cm, corresponding to about 3 to 5 cm into the spleen.

The spleen was punctured under local anaesthesia with the lungs fully expanded, in accordance with MOESCHLIN's (1947) recommendation. We noticed that elderly persons do not always take such a deep breath on one occasion as on another; before examination, the patient should, therefore, under fluoroscopic control, practice taking as deep a breath as possible and holding it. In order to avoid injury to the pleura the needle should be directed slightly dorsally and cranially from the site of puncture in the mid-axillary line. Although we sometimes felt the scrubbing sensation of the spleen passing back and forth over the tip of the needle during the respiratory cycle, as reported by MOESCHLIN and others, we gained the impression that this occurred only when the spleen was enlarged.

Contrast media. We used 30 ml of Umbradil 'Astra' (Diodonum) 50 % and, in some cases, a similar dose of Triurol 'Leo' (Sodium Acetrizoate) 50 %.

As most other investigators (SOTGIU et coll. 1952, COOPER et coll. 1953, GVOZDANOVIĆ et coll. 1953) we found an injection rate of 6 to 7 ml/sec to be the most suitable, but, unlike BOULVIN et coll. (1951) and LEGER et coll. (1953), we did not find it necessary or even advisable to check the position of the needle under fluoroscopic control. Such a measure would necessarily mean respiration with the needle in the spleen and consequently involve a greater risk of injury to the organ than with the puncture performed during apnoea.

The first film was obtained 1 second after the beginning of the injection and subsequent films at intervals of 1.4 sec. Such serial films show not only the passage of the contrast medium through the entire portal system, but also the direction of flow in various portions of the vessels. In addition, such a series always includes at least one film with optimal filling of the vessels and one with optimal accumulation of contrast medium in the liver parenchyma. Furthermore, the use of a cassette changer helps to standardize the conditions for assessing how fast the contrast medium leaves the portal system

(ABEATICI et coll. 1952). The needle is withdrawn immediately after the injection of the contrast medium. One minute after the termination of the injection, a supplementary film is taken to check whether any of the contrast medium has passed up the track of the needle and become entrapped under the capsule of the spleen (subcapsular contrast reflux).

It is apparent from Diagram 1 that the occurrence of subcapsular contrast reflux varies with the rate of injection and the distance between the tip of the needle and the hilum of the spleen (as measured in the roentgenograms). It is evident that, if reflux is to be avoided, the contrast medium should not be injected at a rate exceeding 7.5 ml/sec.

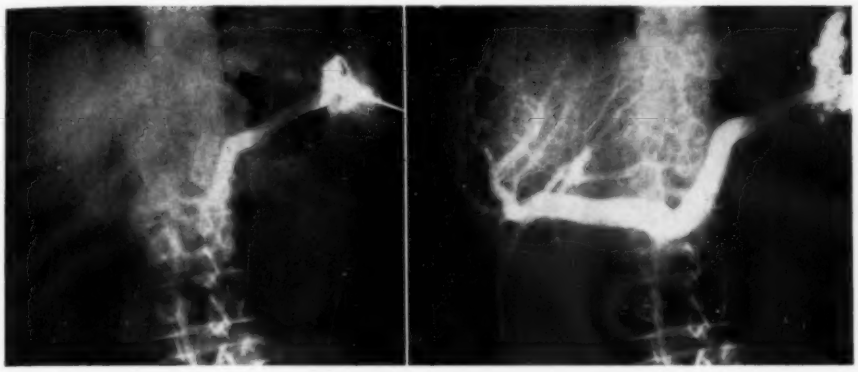
Exposure data. F. F. D. 100 cm, 500 mA, 70 to 100 kV, 0.10 to 0.30 sec. Lysholm grid; normal-speed intensifying screens.

Subjective and objective reactions and complications

The blood pressure and the pulse rate were measured immediately before and after the examination and only slight differences noted. Most of the patients experienced no discomfort after the examination. On 3 occasions, the injection was followed by transient nausea and, in 10 others, by a 'stitch' of 10 minutes' to 6 hours' duration in the left flank. The severity of the symptoms in these 10 cases varied with the amount of contrast medium which, owing to imperfect technique, had been deposited just underneath the splenic capsule or in neighbouring parts of the abdominal cavity. When, during the course of the injection, the pressure at the tip of the needle increases, the contrast medium seeks the line of least resistance, which, if the tip of the needle is near the hilum, is towards the veins. But the rate at which the splenic vein can cope with such an addition is limited. If the rate of injection exceeds this limit, part of the excess contrast medium will, as mentioned earlier, flow up the track of the needle. If the injection is properly performed, only a small spot of contrast medium should be demonstrable in the parenchyma after withdrawal of the needle, and then only at the site of the tip of the needle during injection (Diagram 1).

Appreciable reflux occurred in 10 of the 31 examinations. In one case the patient took a much deeper breath than when the routine plain film for determining the position of the spleen was taken. The result was that the contrast medium was deposited in the left pleural cavity. This was followed by a few hours' pain in the flank but the patient felt well the following day when a small amount of fluid was demonstrable in the left pleura. In another case, the puncture was too deep and resulted in the injection of the contrast medium into the abdominal cavity. Apart from a 'stitch' in the left flank for 5 to 6 hours the patient experienced no discomfort.

The side-effects and complications described above were the only ones recorded in the present series.



a. b.

c.

Fig. 1. Case 1. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 4 sec.): Normal portal system. a. 1 sec.; b. 4 sec. after beginning of injection; c. 4 sec. after end of injection.

Results

A. *The normal portal system.* In 9 cases, the roentgenograms showed no signs of anatomic changes or disturbed function of the portal system. Subsequent laparotomy and histologic examination of a biopsy specimen of the liver was performed in 6 of these 9 cases and likewise failed to reveal any signs of disease involving the portal system. One of these cases is briefly described below.

Case 1. S. 760406. Woman, aged 78, admitted because of one month's jaundice without pain. Liver function tests suggested biliary stasis without involvement of the parenchyma.

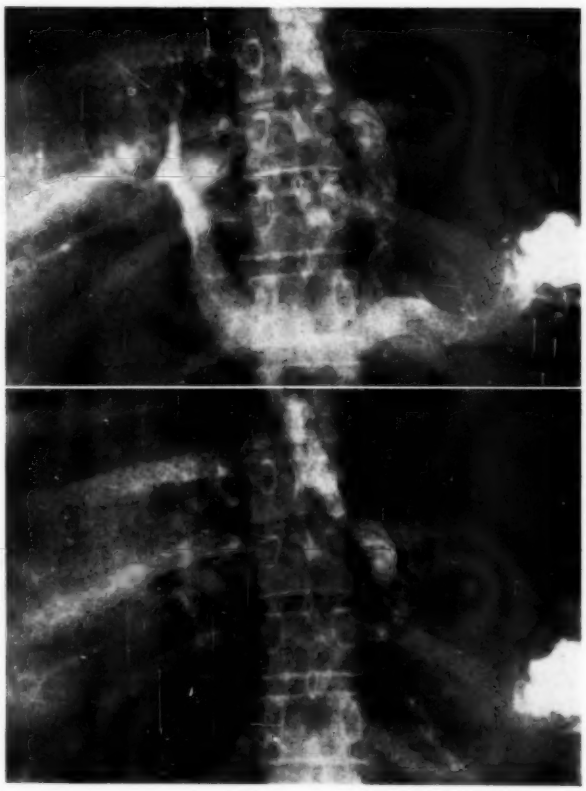
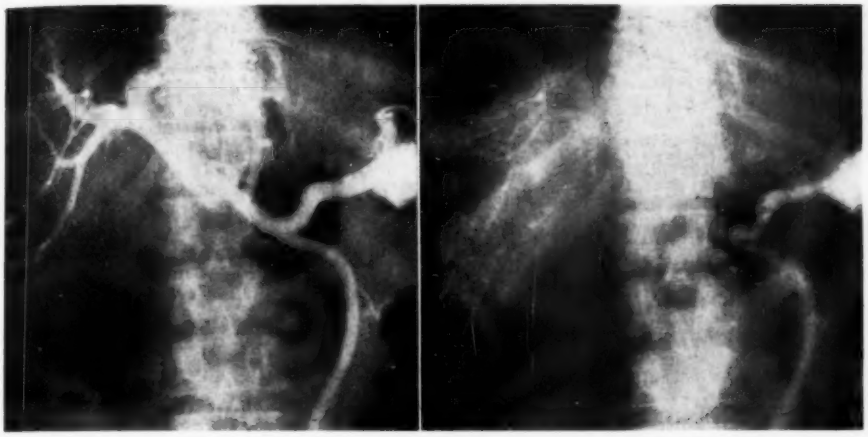


Fig. 2. Case 2. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 4 sec.): Liver cirrhosis, mural thrombosis on the right side of the portal vein and filling of collateral veins. a. 4 sec. after beginning of injection; b. 3 sec. after end of injection.

Percutaneous lieno-portal venography (Fig. 1). Good filling was obtained of the splenic and the portal vein, both of which were of normal appearance. A small defect in the contrast column marked the junction of the splenic vein with the superior mesenteric vein. No signs of collaterals were evident. The arrangement of the intrahepatic branches was regular and they tapered off evenly. Film taken 3 sec. after the end of the injection showed an even accumulation of contrast medium in the liver parenchyma and a small amount of contrast medium, which had passed from the hilum out towards the capsule of the spleen (subcapsular reflux).

Laparotomy revealed a carcinoma at the papilla Vateri. The tumour was about 2 cm in diameter and not large enough to displace any of the vessels. The liver was slightly enlarged and microscopic examination showed biliary stasis but no other evidence of disease.



a. b.

Fig. 3. Case 3. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 5 sec.): Liver cirrhosis with filling of collateral veins. a. 4 sec. after beginning of injection; b. 4 sec. after end of injection.

B. *The portal system in portal hypertension.* On 8 occasions examination revealed signs of intrahepatic obstruction with filling of collateral veins. Liver cirrhosis was demonstrated in 7 cases examined histologically. In these 7 cases, the portal pressure, as measured at operation, was increased (290 to 550 mm H_2O) (EKMAN & SANDBLOM 1954).

In 3 of these cases, a filling defect was seen along the wall of the portal vein — thrombosis —, a finding verified at operation. An example is given below.

Case 2. S. 080501. Woman, aged 46, with posthepatitic cirrhosis, ascites and signs of portal hypertension. Roentgen examination of the esophagus revealed large varices.

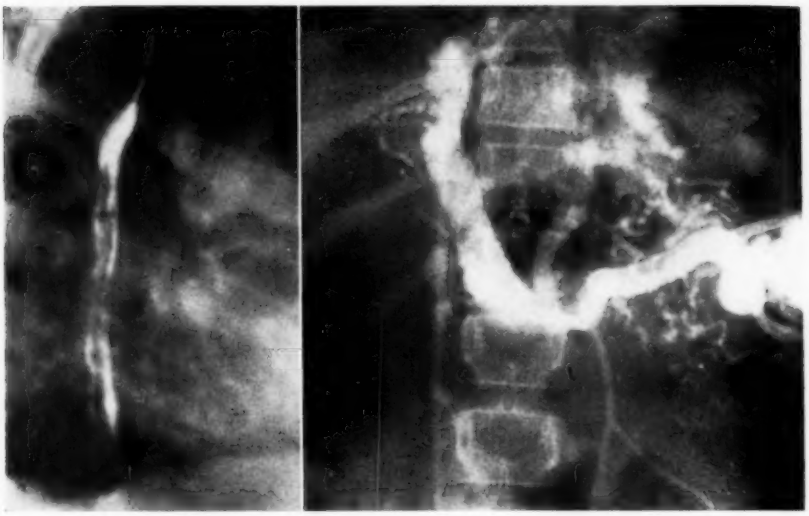
Percutaneous lieno-portal venography (Fig. 2). The intrahepatic portal branches were sparse, tortuous and tapered rapidly. At the bifurcation of the portal trunk was a filling defect — thrombosis. The size of the liver was diminished. Filling of the coronary vein up towards the esophagus occurred.

Operation (porta-caval shunt — all the porta-caval shunts were performed by Professor PHILIP SANDBLOM) verified both the presence of cirrhosis and the thrombus.

The demonstration of intrahepatic obstruction with the formation of a collateral circulation may be exemplified further by another case.

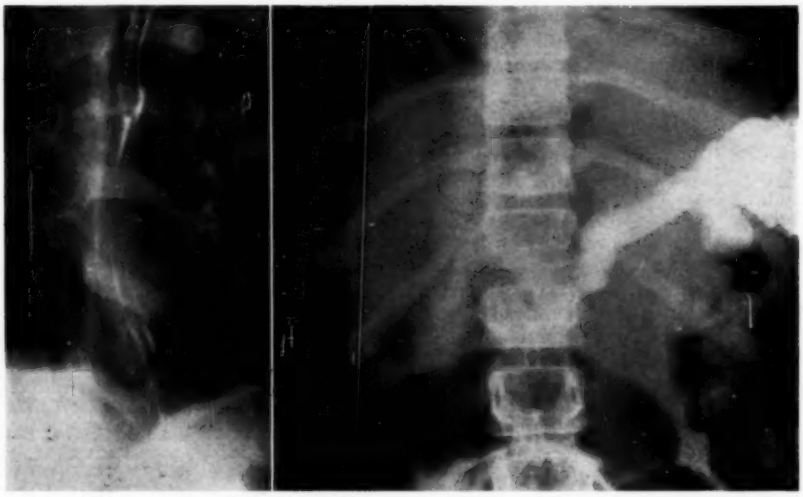
Case 3. M. 020226. Male, aged 52, inveterate alcoholic, who had been admitted for jaundice and increasing ascites of three months' duration. Roentgen examination revealed small varices in the lower portion of the esophagus.

Percutaneous lieno-portal venography (Fig. 3). Filling was obtained of the inferior mesenteric vein and the coronary vein, which emptied into varicose veins at the level



a. b.

Fig. 4. Case 4 before operation. a. Esophagus: varices in the lower portion. b. Percutaneous lieno-portal venography (30 ml Umbradil 50 %, 4 sec. after beginning of injection): Liver cirrhosis with occlusive thrombosis of the portal vein; filling of collaterals.



a. b.

Fig. 5. Case 4 3 weeks after operation. a. Esophagus: regression of the varices. b. Percutaneous lieno-portal venography (30 ml Umbradil 50 %, 6 sec. after beginning of injection): Normally functioning porta-caval shunt; no filling of collaterals.

of the cardia. The liver was markedly reduced in size. The small intrahepatic branches were sparser than usual, otherwise nothing pathologic was noted.

The patient was not operated upon. He probably had a small nodular cirrhosis of the liver which had only slightly affected the roentgen appearance of the large portal branches. However, the portal bed was presumably so reduced as to lead to the formation of collaterals.

In five of the patients with cirrhosis and portal hypertension, percutaneous lieno-portal venography was performed also after porta-caval shunt (in one of them on 2 occasions) for controlling the function of the anastomosis. No collaterals could be seen and the contrast medium flowed through the anastomosis out into the inferior cava in all of these cases, an example of which is given below.

Case 4. S. 431028. A girl, aged 10, with posthepatitic cirrhosis was admitted because of ascites and alarming hematemesis. Roentgen examination of the esophagus before operation revealed moderate varices (Fig. 4 a).

Percutaneous lieno-portal venography before operation (Fig. 4 b). Total occlusion of the main branches of the portal vein in the liver hilum with filling of the collaterals both cranially towards the esophagus via the coronary vein and caudally via the inferior mesenteric vein.

At operation (porta-caval shunt) pronounced liver cirrhosis with a thrombus at the bifurcation of the portal vein was seen. Three weeks after operation roentgen examination showed regression of the varices (Fig. 5 a).

Percutaneous lieno-portal venography after operation (Fig. 5 b). The collaterals had disappeared. Contrast medium could be seen in the inferior caval vein thus demonstrating a functioning anastomosis.

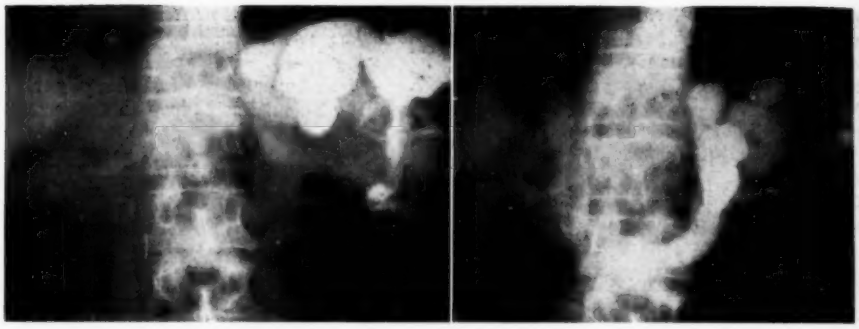
In one case (in which the patient was examined twice) percutaneous lieno-portal venography suggested a thrombus in the splenic vein.

Case 5. S. 040424. Man, aged 50, who had been submitted elsewhere to laparotomy because of acute gastric hemorrhage. Although palpation of the stomach had revealed no signs of a pathologic condition, several dilated veins, suggesting portal hypertension, had been observed in the pyloric region. The liver had been regarded as slightly cirrhotic. The abdomen was closed and the patient referred to the Department of Surgery, Lund, for further investigation and treatment. The investigation there showed normal liver function, splenomegaly and signs of hypersplenism. Roentgen examination of the esophagus and stomach revealed large filling defects, suggestive of varicose veins, at the fundus of the stomach.

Percutaneous lieno-portal venography (Fig. 6). The spleen was punctured at a fairly high level. No filling was obtained of the main branch of the splenic vein, but the contrast medium passed via severely dilated venae gastricae breves into a varicose entanglement at the fundus of the stomach. The contrast medium then flowed slowly into a dilated vein in which it was markedly diluted and discharged into a large vessel extending in a cranial direction. A filling was obtained of the left gastro-epiploic vein.

Re-examination, at which the spleen was punctured at mid-level, gave the same findings.

During operation a roentgenogram was obtained with a catheter introduced into one of the branches of the superior mesenteric vein (Fig. 7). The portal vein was of normal width and showed no signs of obstruction. Biopsy specimen of the liver: no evidence of cirrhosis. Taken together, the observations made at these examinations suggested thrombosis of the splenic vein.

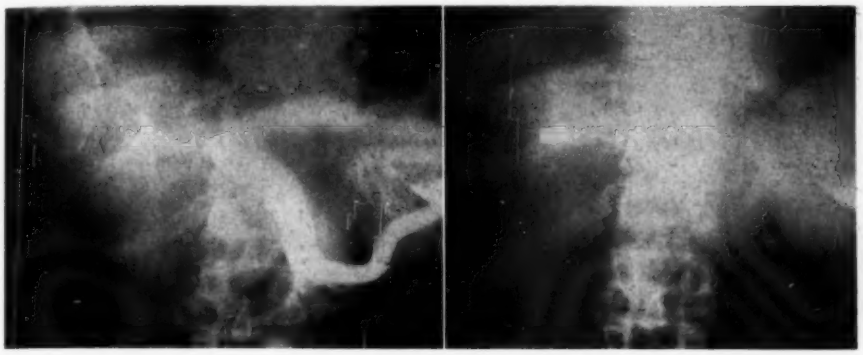


a. b.

Fig. 6. Case 5. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 5 sec.): Thrombosis of the splenic vein with collateral circulation. a. 5 sec. after beginning of injection; b. 7 sec. after end of injection.

Fig. 7. Case 5. Portal venography: the contrast medium was deposited via a catheter into a branch of the superior mesenteric vein during operation. Portal vein of normal width.

The visible distal portion of the splenic vein which contained no palpable thrombus appeared to be of normal width, but the blood in it flowed towards the spleen, probably because some of the pancreatic veins emptied into the splenic vein distal to the obstruction. The venous pressure was found to be 290 mm H_2O. Splenectomy and splenorenal anastomosis were therefore performed.



a. b.

Fig. 8. Case 6. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 5 sec.): Tumour of the right lobe of the liver encroaching upon the right portal branch (primary carcinoma of the liver). a. 4 sec. after beginning of injection; b. 5 sec. after end of injection.

C. *The portal system in the presence of a liver tumour.* In 3 cases, roentgen examination revealed signs of expansive growths in the liver. In all of these 3 cases, the diagnosis was verified at laparotomy.

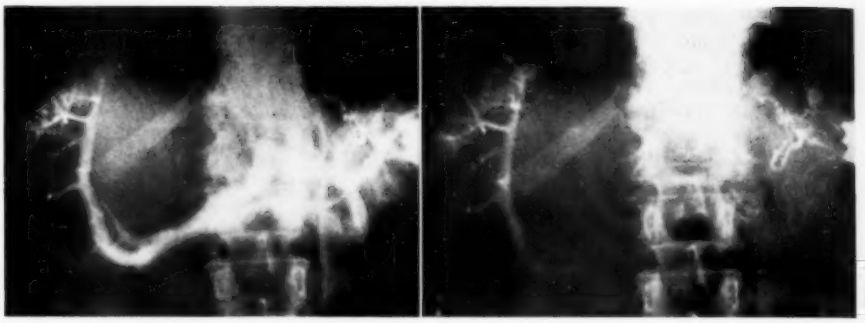
Case 6. Th. 920328. Man, aged 62, with a history of 4 to 5 months' increasing loss of weight and pain in the right flank. Aortography revealed an expansive process in the right lobe of the liver.

Percutaneous lieno-portal venography (Fig. 8). The main branch of the portal vein was displaced in a cranial direction. The right branch ended abruptly just after the division of the portal vein, suggesting encroachment of the tumour, while the left lobe of the liver showed a normal vascular pattern and was slightly enlarged. A pronounced accumulation of contrast medium was seen in this lobe (Fig. 8 b).

The roentgen diagnosis was verified at laparotomy. In addition the surface of the left lobe of the liver was studded with small tumours which contra-indicated the intended resection of the right lobe. Microscopic examination of a biopsy specimen showed primary carcinoma of the liver.

Case 7. M. 870412. Woman, aged 67, with one month's history of loss of appetite and epigastric pain, and with a palpable lump under the right costal arch.

Percutaneous lieno-portal venography (Fig. 9). Good filling was obtained of the splenic vein and the portal vein. The latter was displaced cranially. The main branches of the portal vein were pushed apart by an expansive process in the medial part of the right lobe of the liver, in which no portal veins were to be seen. The smaller vessels, given off laterally and caudally by the right portal branch, were sparse and straighter than usual, and thus suggested expansive, avascular processes in this region as well. Destruction of the liver parenchyma was evidenced by the persistence of the contrast medium in the right portal branch 9 seconds after the end of the injection. In this case no accumulation of contrast medium was observed in the parenchyma. Microscopic examination of a biopsy specimen showed a primary tumour of the liver. (Malignant angioendothelioma.)



a. b.

Fig. 9. Case 7. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 4 sec.): Multiple cystic tumours of the liver (angio-endothelioma). a. 5 sec. after beginning of injection; b. 6 sec. after end of injection.

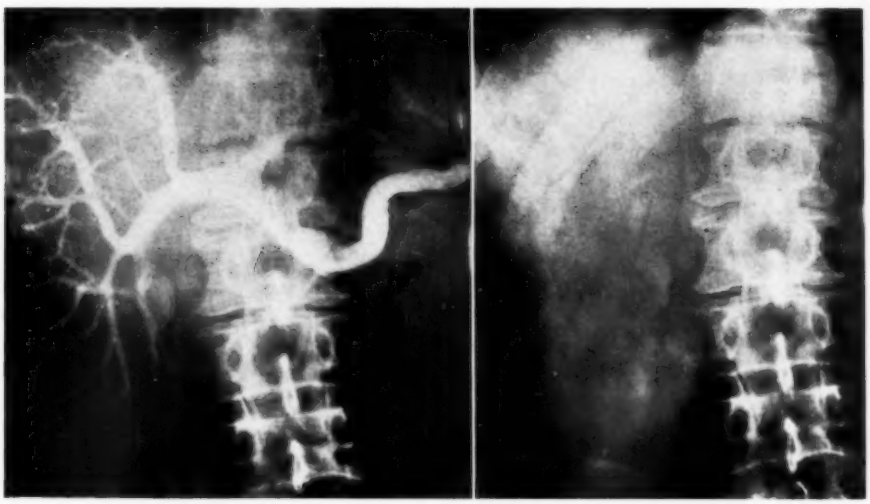


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Fig. 10. Case 8. Percutaneous lieno-portal venography (30 ml Umbradil 50 %. Injection time 5 sec.): Tumour in the middle and left parts of the liver (primary carcinoma of the liver). a. 5 sec. after beginning of injection; b. 6 sec. after end of injection.

Case 8. S. 900110. Man, aged 64, was admitted because of a painful lump in the right epigastrium.

Percutaneous lieno-portal venography (Fig. 10). The portal vein was slightly displaced in a cranial direction. The right portal branch presented ordinary appearances, but the left gave off no branches. The middle and left part of the liver showed poor accumula-

tion of contrast medium, as compared with the normal right lobe. The liver was slightly enlarged. On explorative laparotomy, a large tumour was seen in the central part of the liver. Microscopic examination of a biopsy specimen revealed a primary carcinoma of the liver.

The examination failed on 3 occasions because of unsuccessful puncture.

Discussion

In 10 of the 31 examinations the long axis of the spleen, as seen in the preliminary roentgenogram, measured at the most 15 cm, which was regarded as the upper normal limit. In 8 of these cases, the contrast medium was injected into the spleen. In one case, it was inadvertently injected into the pleura and in another into the abdominal cavity. Good filling of the portal system was obtained in 7 of these 8 cases. In the remaining case, the tip of the needle was so far away from the hilum that the veins did not receive sufficient contrast medium.

Many investigators, such as DREYER & BUDTZ-OLSEN (1952) and MILNES WALKER (1953), reported that they only examined patients with enlarged spleens. Judging by the reproductions published by other authors, ABEATICI et coll. and LEGER appear to be the only ones who have obtained roentgenograms of satisfactory quality after puncture of apparently normal-sized spleens. In this connection, a satisfactory roentgenogram is to be understood as one permitting not only evaluation of the morphology of the portal trunk, but also of the pattern of its intrahepatic branches and of the accumulation of contrast medium in the liver parenchyma. On the other hand, in none of our cases was a filling obtained of the hepatic veins, but it is possible that this can be obtained by the use of a more concentrated contrast medium. But then the risk of thrombophlebitis of the splenic vein and of injury to the liver cells must be considered.

Judging by observations made in the present study, the normal pattern of the intrahepatic branches and the pattern seen in cirrhosis are in good agreement with the descriptions given by MCINDOE (1928) and HJORTSJÖ (1948), based on autopsy studies, and by CACCIARI & FRASSINETI (1953), based on clinical venographic studies. In the presence of advanced cirrhosis the main branches taper rapidly and run an irregular, tortuous course. The smaller branches are sparser than usual and taper rapidly. Like LEGER (1951) and DREYER & BUDTZ-OLSEN (1952), we were unable to confirm MOORE & BRIDENBAUGH's (1951) claim that the blood from the splenic vein generally flows to the left part of the liver.

Cirrhotic degeneration of the liver parenchyma gradually occludes the intrahepatic portal branches with consequent portal hypertension (KELTY, BAGGENSTOSS & BUTT 1950). In 3 of our cases, the passage of

contrast medium in the larger portal branches was partly or completely obstructed at the liver hilum (Figs. 3 and 4 b). At operation, the obstruction was found to consist of a mural thrombus extending towards the liver.

As to the rate of flow of the contrast medium, we noticed that with one and the same injection technique the presence of cirrhosis slowed the passage of contrast medium through the liver. Furthermore, we observed that the collaterals were still filled with contrast medium long after the contrast medium had disappeared from the portal vein. This suggests that the flow through the collateral circulation is even slower than through the cirrhotically degenerated part of the liver. The findings at percutaneous lieno-portal venography of the direction of flow through the collaterals from the portal system to the caval system is a true reproduction of a patho-physiologic state indicated by the observation that the contrast medium persisted longest in that part of the collaterals nearest the caval system. Observations made in the present investigation suggested that, with the technique used, the contrast medium is never introduced into the portal system under a pressure exceeding that already existing, so that no portion of the vessels will ever be filled against the flow of blood. In no instance was a filling obtained of the superior mesenteric vein, not even when the portal vein was completely occluded (Fig. 4 b). On the other hand, it was clearly observed that the contrast medium was diluted as it flowed towards its discharge.

As mentioned earlier, demonstration of the direction of flow in various segments of the veins requires serial roentgenograms.

Like COOPER et coll. (1953) and MILNES WALKER et coll. (1953), we found percutaneous lieno-portal venography an excellent medium for assessing the functioning of a porta-caval shunt. The roentgenograms not only show the functioning anastomosis, but indicate by the lack of filling of the collaterals that the flow of blood through them is reversed to normal owing to the decrease in portal tension.

It appears that percutaneous lieno-portal venography, if properly performed, is a good examination method involving but slight risks of complication. It may be employed in the investigation of known or suspected expansive processes involving the splenic vein or the portal vein and in the investigation of probable expansive processes in the liver.

The method can also give valuable information in the investigation of suspected obstruction in any segment of the portal system, especially regarding the site of such obstruction, and thereby facilitate the choice of operation.

Finally, percutaneous lieno-portal venography is useful for checking the functioning of a porta-caval shunt and thereby also for predicting the prognosis.

SUMMARY

The technique of percutaneous lieno-portal venography and the range of indications of the method as well as the occurrence and prevention of complications are described. Observations made on the basis of 31 examinations suggested that this method gives important information on the anatomy and physiology of the portal system, and is valuable, not only for diagnosing portal hypertension and assessing the effectivity of a porta-caval shunt, but also for diagnosing liver tumours. No serious complications occurred.

ZUSAMMENFASSUNG

Die Technik der perkutanen lieno-portalen Venographie, die Indikationen der Methode und Vorkommen und Verhütung der Komplikationen werden beschrieben. Die Beobachtungen nach 31 Untersuchungen erweckten diese Folgerungen: Die perkutane lieno-portale Venographie gibt wertvollen Bescheid über die Anatomie und Physiologie des Pfortadersystems. Sie ist von grossem Wert nicht nur um portalen Hochdruck zu diagnostizieren und die Effektivität der porta-cavalen Verbindung festzustellen, sondern auch um Lebertumoren zu diagnostizieren. Keine grösseren Komplikationen kamen vor.

RÉSUMÉ

Les auteurs décrivent la technique de la phlébographie spléno-portale transpariétale, les indications de la méthode, l'existence de complications et leurs procédés de prévention. Les résultats de 31 examens ont conduit aux conclusions suivantes: la phlébographie spléno-portale transpariétale a un grand intérêt pour la connaissance de l'anatomie et de la physiologie du système porte. Elle est aussi d'une grande valeur pour diagnostiquer les cas d'hypertension portale et pour préciser le fonctionnement d'une anastomose porto-cave, mais aussi pour diagnostiquer les tumeurs du foie. Cette méthode n'a pas entraîné de grosses complications.

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ÄQUIVALENTE AUFNAHMEBEDINGUNGEN IN DER RÖNTGENDIAGNOSTIK

von

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1. Problemstellung

Für die Praxis im diagnostischen Betrieb ist es oft von gewisser Bedeutung, die Einstellgrössen am Röntgenapparat für eine bestimmte Aufnahme bei unterschiedlichen Einstellbedingungen miteinander zu vergleichen. Dieser Vergleich kann sich dabei entweder auf das für eine bestimmte Filmschwärzung erforderliche mA-sec-Produkt bei verschiedenen Spannungen an der Röntgenröhre beziehen, oder auf einen Vergleich der erforderlichen Belichtungsgrössen an verschiedenen Apparate-Typen, z. B. Drehstrom- und Vierventil-Apparaten. In beiden Fällen ist natürlich unter äquivalenten Aufnahmebedingungen etwas Verschiedenes zu verstehen. Im ersten Fall kann sich die Äquivalenz nur auf die gleiche mittlere Filmschwärzung beziehen, während es im zweiten Fall sinnvoll ist, die beiden zu vergleichenden Aufnahmen dann als äquivalent zu bezeichnen, wenn sie ausser der gleichen mittleren Filmschwärzung auch gleichen Bildcharakter (d. h. gleiche Kontraste) haben. Diese Probleme sind verschiedentlich in der Literatur behandelt worden. Ich möchte, ohne Vollständigkeit zu beanspruchen, für den ersten Fall auf die Arbeiten von BIERMAN und BOLDINGH (1) und SCHOBER (5), für den zweiten Fall auf die Untersuchungen von MEILER (2) hinweisen.

Im folgenden sollen nun diese Vergleiche auf Grund neuer experimenteller Ergebnisse zusammenfassend dargestellt werden. Zur Beschreibung der Messergebnisse werden zwar mathematische Ausdrücke benutzt, man muss sich jedoch von vornherein darüber klar sein, dass keine der angegebenen Beziehungen beanspruchen kann, ein Naturgesetz darzustellen; alle diese Ausdrücke sind vielmehr Näherungsformeln, die in dem untersuchten Filter- und Spannungsbereich die experimentellen

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Werte im Rahmen der Messgenauigkeit wiedergeben. Eine exakte theoretische Beschreibung müsste von der spektralen Energieverteilung der Röntgenstrahlen ausgehen; zunächst wäre dann das Spektrum nach Schwächung durch das Objekt zu bestimmen, dann die Fluoreszenz-Ausbeute dieses Spektrums in der Verstärkerfolien-Kombination. Aus der Intensität des Fluoreszenzlichtes der Folie ergäbe sich dann die Schwärzung auf dem Röntgenfilm. Man sieht sofort, dass dieses Verfahren so umständlich ist, dass die Ergebnisse in keinem Verhältnis zu dem Aufwand stehen würden. Andererseits ist die Genauigkeit einer exakten theoretischen Behandlung auch nicht erforderlich, da in der Praxis eine Genauigkeit und Reproduzierbarkeit von einigen Prozent schon kaum zu erreichen und einzuhalten ist. Wenn man den vorher angedeuteten Weg geht, dass man möglichst einfache mathematische Ausdrücke sucht, die die Messergebnisse im Rahmen ihrer Fehlergrenzen wiedergeben, so kann man dabei nicht erwarten, dass man zu einer in sich widerspruchslosen Theorie gelangt. Man muss sich also bei der Verwendung jeder der angegebenen Formeln überlegen, ob die erwarteten Aussagen nicht über ihren Geltungsbereich hinausgehen.

2. Experimentelle Ergebnisse

a) *Filmschwärzung.* Für die beabsichtigten Vergleiche muss man von reiner Gleichspannung ausgehen, da man nur so zu einwandfreien, definierten Resultaten kommen kann. (Benutzt wurde ein Tiefentherapie-Apparat (Müller RT 200). Die maximale Welligkeit bei den Aufnahmen betrug 4 kV. Das Eigenfilter von Röntgenröhre und Röhrenschutzgehäuse war äquivalent zu 3 mm Aluminium.) Zunächst sind die zur Erreichung einer bestimmten Schwärzung, z. B. $S = 1$, erforderlichen Belichtungsgrössen in Abhängigkeit von der Spannung für verschiedene Objekte zu bestimmen. Sei etwa J die Belichtungsgrösse, d. h. J soll ein Mass für die filmschwärzende Lichtmenge der verstärkenden Folie sein; dann ist der Zusammenhang zwischen der Filmschwärzung S und der Grösse J oberhalb einer bestimmten Schwärzung durch

$$S = \gamma \cdot \log J \tag{1}$$

gegeben. Die nächste Aufgabe ist also, die Grösse J als Funktion der Röhrenspannung und des durchstrahlten Objektes zu bestimmen. Dabei kann es sich nicht darum handeln, J etwa in absoluten Zahlen anzugeben, da die zur Erzielung etwa einer gleichen Schwärzung $S = 1$ erforderliche Belichtungsgrösse von dem benutzten Film abhängt. Andererseits hat es auch keinen Sinn, unter Beschränkung auf ein Filmfabrikat die erforderlichen mAs-Produkte anzugeben, da diese z. B. von dem jeweiligen Aufnahmeabstand und der Strahlenausbeute der Röhre abhängen. Man kann daran denken, wenigstens den Film aus der Reihe der Variablen aus-

zuschalten, indem man Dosismessungen zu Grunde legt, wie MEILER es tut. Dieses Verfahren ist zwar messtechnisch relativ einfach, hat jedoch den schwerwiegenden Nachteil, dass das Verhältnis zwischen der Dosis und der oben eingeführten Belichtungsgrösse von der Röhrenspannung und der Filterung durch das Objekt abhängt, d. h. von der Qualität der Strahlung, was bei der erheblichen Filterung, die das Kalzium-Wolframat der Verstärker-Folie darstellt, nicht weiter verwunderlich ist. Darüber hinaus ist es aus dem gleichen Grunde schwierig, das Aluminium-Äquivalent (MEILER benutzen für seine Messungen Aluminium als Schwächungssubstanz) der medizinischen Objekte zu bestimmen. Wir schliessen uns deshalb im Prinzip dem Vorgehen von HONDIUS-BOLDINGH an, der die Abhängigkeit der Grösse J von der Röhrenspannung durch Aufnahmen medizinischer Objekte bestimmt und zu folgender Darstellung gelangt:

$$J = K \cdot Q \cdot U^p \qquad (2)$$

(Q = mAs-Produkt; U = Röhrenspannung) wobei sich für den Exponenten p der Wert 5 ergibt. Der Proportionalitätsfaktor K hängt von dem Objekt, sowie der Film- und Folienempfindlichkeit ab.

Wir haben nun, um die Abhängigkeit zwischen der Belichtungsgrösse J, der Röhrenspannung U und dem Objekt genau zu bestimmen, Aufnahmeserien mit verschiedenen Verstärkerfolien durchgeführt. Das Verfahren war folgendes: Mit dem Scheiner-Rad wurden Gradationskurven aufgenommen. (Scheiner-Rad ist eine Sensitometerscheibe; bei der Aufnahme werden verschiedene Teile des Films verschieden lange Zeiten der Röntgenstrahlung ausgesetzt, so dass man mit *einer* Belichtung eine ganze Gradationskurve aufnehmen kann.) Bei allen Aufnahmen wurden der Fokus—Film-Abstand, der Röhrenstrom und die Belichtungszeit konstant gehalten. Als Filter benutzten wir Wassersäulen von 4 bis 30 cm. Der Abstand zwischen der Wassersäule und dem Film wurde so gross gemacht und das Strahlenbündel so klein gehalten, dass der Anteil der Streustrahlung aus dem Wasser vernachlässigbar war. (Fokus—Film-Abstand = 150 cm; Objekt—Film-Abstand = 100

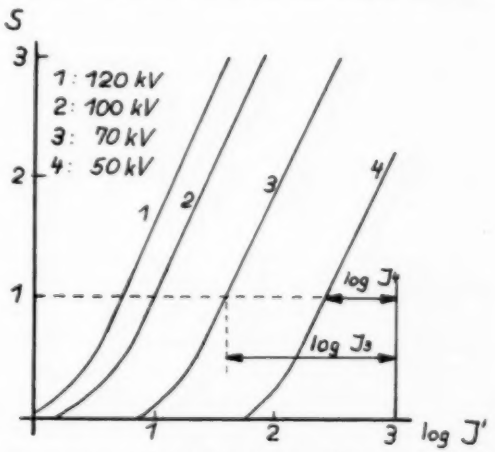

Diagramm 1. Gradationskurven für verschiedene Spannungen bei gleichen mAs. Universal-Folie; 10 cm H_2O.

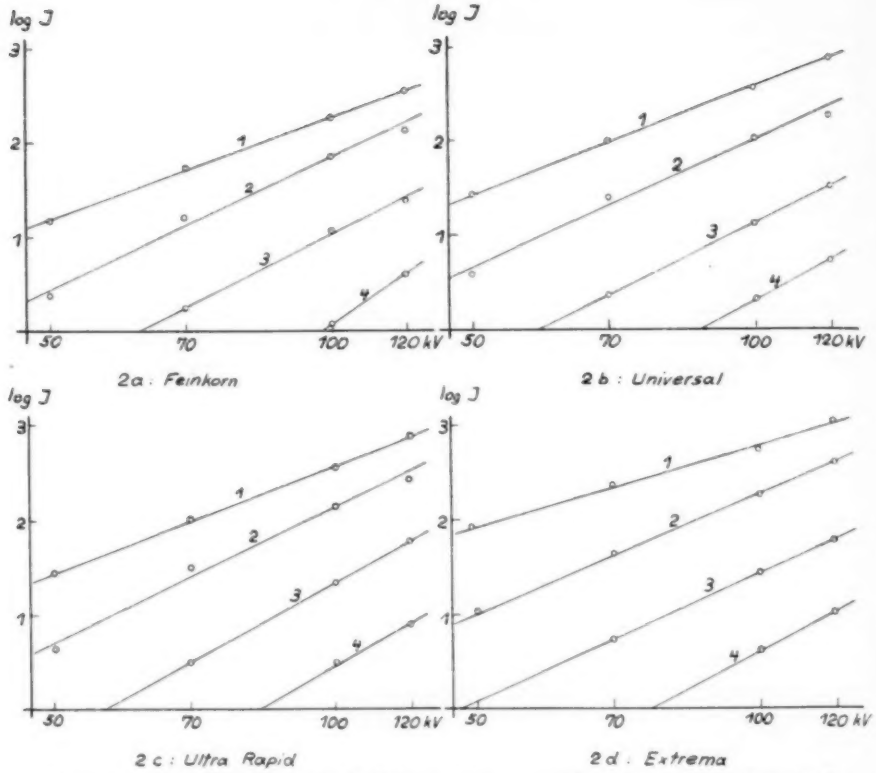

Diagramm 2. Abhängigkeit der Belichtungsgrösse von der Spannung: 1: 4 cm H_2O; 2: 10 cm H_2O; 3: 20 cm H_2O; 4: 30 cm H_2O.

cm; Objekt-Durchmesser = 7 cm.) Die dargestellten Ergebnisse entsprechen also den Verhältnissen bei Aufnahmen mit idealen Streustrahlenblenden. Für die Aufnahmen wurden vier Folien-Kombinationen von Cawo benutzt: eine Feinkorn-, eine Universal-, eine Ultra-Rapid- und eine Extrema-Folie. Alle Aufnahmen wurden mit jeder Folie durchgeführt. Die Aufnahmen wurden gruppenweise entwickelt, wobei durch eine jeweils mitentwickelte Testaufnahme sichergestellt wurde, dass die Entwicklungsbedingungen unverändert geblieben waren.

In Diagramm 1 sind einige der erhaltenen Gradationskurven wiedergegeben, wobei wie üblich die Schwärzung S über dem dekadischen Logarithmus der Belichtungsgrösse aufgetragen ist. Die für die folgenden Darstellungen benötigte Belichtungsgrösse J, die sich auf normale Aufnahmen ohne Scheiner-Rad bezieht, erhält man nun, wenn man von

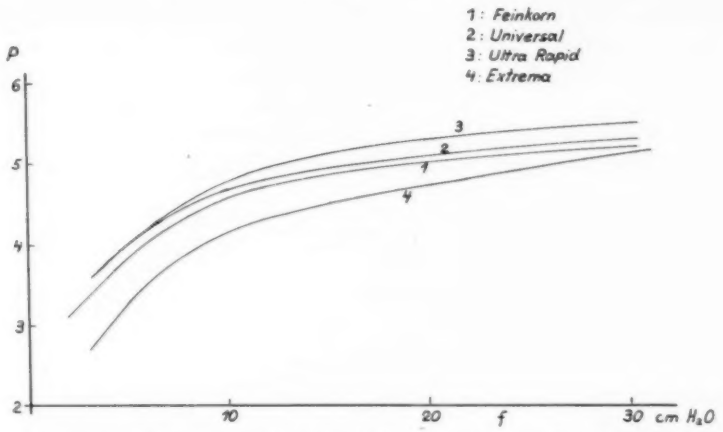

Diagramm 3. Zusammenhang zwischen p und dem Wasserfilter f.

einem willkürlichen Bezugspunkt auf der Abzsisse ausgehend, als den wir log $J' = 3$ genommen haben, die Strecke bis zu der Abzsisse, bei der die Schwärzung z. B. $S = 1$ ist, misst. Diese Strecke ist gleich dem Logarithmus der Belichtungsgrösse J (in willkürlicher Einheit) bei irgendeinem, aber festgehaltenen, mAs-Produkt. Für gleiche Schwärzung muss bei verschiedenen Aufnahmen das mAs-Produkt also zu J umgekehrt proportional sein. Die so erhaltenen Messpunkte sind für die 4 benutzten Folien-Kombinationen in Diagramm 2 als Funktion der Röhrenspannung in doppelt logaritmischen Koordinaten eingetragen. Parameter ist die Höhe der Wassersäule. Man sieht sofort, dass die Messpunkte in recht guter Näherung auf Geraden liegen, was nichts anderes bedeutet, als dass die Beziehung (2) praktisch erfüllt ist. Allerdings ist p nicht konstant, sondern hängt von der Dicke des durchstrahlten Objektes ab. Dies ist zu erwarten, weil die Strahlung durch die Filterwirkung der Wassersäule wesentlich härter wird, und der Anstieg der Energieausbeute (oder auch der Dosisleistung) mit der Spannung umso rascher von statten geht, je stärker das Filter ist. (Siehe z. B. auch 2.) In Diagramm 3 ist p als Funktion der Dicke der durchstrahlten Wasserschicht »f« angegeben. Während die Kurven für die Feinkorn-, Universal- und Ultra-Rapid-Folienkombination so wenig voneinander abweichen, dass man in der Praxis für alle drei Kombinationen eine mittlere Kurve verwenden darf, weicht die Kurve für die Extrema-Folienkombination wesentlich von diesem Verlauf ab. Die letztere Folie ist also offensichtlich grundsätzlich anders aufgebaut als die anderen Folien.

Diese Ergebnisse reichen aus, um bei Gleichspannungs-Apparaten die

erforderlichen Belichtungsgrössen bei verschiedenen Spannungen ineinander umrechnen zu können. Als Nebenergebnis erhalten wir noch die relativen Belichtungsgrössen für verschiedene Folienkombinationen, die beispielsweise für ein Objekt von 10 cm Wasser (etwa Thorax) in der Tabelle zusammengestellt sind. Als Bezugswerte sind die Belichtungsgrössen für die Universal-Folie bei jeder Spannung jeweils gleich 1 gesetzt:

kV	Feinkorn	Ultra-Rapid	Extrema
50	1,60	0,89	0,56
70	1,60	0,80	0,56
100	1,70	0,76	0,56
120	1,75	0,72	0,53

b) *Bildkontrast.* Ausser der Schwärzung ist bei der Röntgenaufnahme der Kontrast von Interesse. Dabei wollen wir uns hier auf Weichteilkontraste beschränken, d. h. wir betrachten nur die Unterschiede in den Belichtungsgrössen hinter verschiedenen Höhen f der Wassersäule. Eine solche Abhängigkeit wird *i. a.* in Form einer Schwächungskurve dargestellt, die sich für homogene Strahlungen durch

$$J = J_0 \cdot 10^{-\mu_{dek} \cdot f} \tag{3}$$

beschreiben lässt. (Durch den Index *dek* soll angedeutet werden, dass hier μ auf die Basis 10 bezogen ist.) Für heterogene Strahlungen, wie sie in der Medizin stets benutzt werden, ist es nicht selbstverständlich, dass Gleichung (3) mit konstantem μ erfüllt ist (vgl. Dosisschwächungskurven). Dann ist der Schwächungskoeffizient μ_{dek}, der als Masszahl für den physikalischen Kontrast verwendet werden kann, als relative Änderung der Belichtungsgrösse J mit der Dicke der durchstrahlten Wasserschicht zu definieren:

$$\mu_{dek} = \frac{\delta \log J}{\delta f} = 0{,}43 \cdot \frac{1}{J} \cdot \frac{\delta J}{\delta f} \tag{4}$$

Es liegt zunächst nahe, in diesem Ausdruck J aus Gleichung (2) einzusetzen, so dass man erhält:

$$\mu_{dek} = \frac{\delta \log K}{\delta f} + \frac{\delta p}{\delta f} \cdot \log U \tag{5}$$

(Der Proportionalitäts-Faktor K hängt auch von f ab.) Dabei kann $\frac{\delta p}{\delta f}$ aus Diagramm 3 entnommen werden. Mit dieser Darstellung ist jedoch der Gültigkeitsbereich des Ausdrucks (2) überschritten. Die Messergebnisse selbst fügen sich zwar mit befriedigender Genauigkeit in den Verlauf von (2) ein, jedoch ist die Übereinstimmung nicht ausreichend zur Bestimmung der in (5) enthaltenen Differential-Quotienten. Es ist daher richtiger, den Schwächungskoeffizienten direkt aus den Messwerten zu

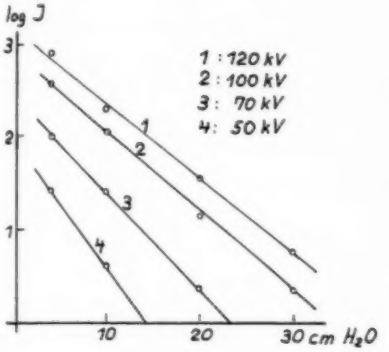

Diagramm 4. Abhängigkeit der Belichtungsgrösse von dem Wasserfilter für verschiedene Spannungen. Universal-Folie.

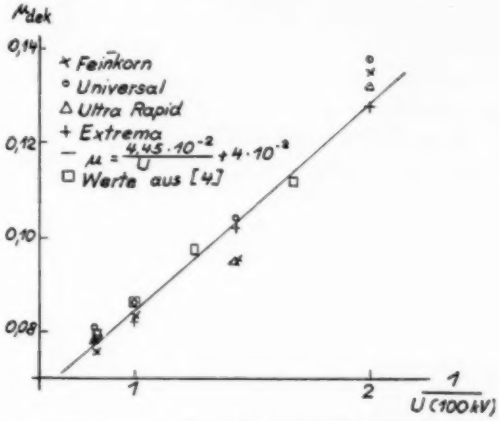

Diagramm 5. Schwächungskoeffizient in Abhängigkeit von der Spannung.

bestimmen, ohne die Näherungsformel (2) zu benutzen. Zu diesem Zweck tragen wir die Messwerte für log J als Funktion von f mit U als Parameter auf, wie dies beispielsweise Diagramm 4 für die Universal-Folie zeigt. Auch hier liegen bei allen verwendeten Folien-Kombinationen die Messpunkte auf Geraden. Es zeigt sich also, dass hier, im Gegensatz zu den Dosisschwächungskurven, die Experimente durch Gleichung (3) dargestellt werden können. Diese Darstellung gilt von $f = 4$ cm bis $f = 30$ cm. J_o ist eine Funktion der Röhrenspannung und der Folienkombination, während μ in der vorliegenden Näherung von f unabhängig ist. Die beiden Gleichungen (2) und (3) sind, wie hier noch betont werden soll, mathematisch nicht miteinander verträglich. Sie stellen also kein Naturgesetz dar, sondern lediglich Näherungen, die für den vorliegenden Zweck in dem untersuchten Bereich der Variablen brauchbare Ergebnisse liefern. Eine genaue Untersuchung der experimentellen Ergebnisse zeigt auch, dass die Kurven in Diagramm 2 leicht konvex nach oben, die Kurven in Diagramm 4 und den entsprechenden Diagrammen für die anderen Folien jedoch schwach konvex nach unten sein müssen. p nimmt also mit zunehmender Spannung bei konstanter Filterung, μ_{dek} mit zunehmender Filterung bei konstanter Spannung leicht ab. Diese Änderungen von p und μ können in den hier behandelten Bereichen von Spannung und Filterung jedoch vernachlässigt werden. Die Bestimmung von μ_{dek} gemäss Diagramm 4 gibt nun die in Diagramm 5 eingetragenen Werte.

Als Abszisse wird hier der Kehrwert der Spannung genommen, da sich zeigt, dass μ_{dek} in guter Näherung in dem untersuchten Spannungs-

bereich als lineare Funktion von $\frac{1}{U}$ angesehen werden kann. Auch hier weichen die Werte von μ_{dek} für die verwendeten Folienkombinationen so wenig voneinander ab, dass man eine mittlere Gerade benutzen kann. Misst man U in 100 kV und μ_{dek} gemäss (3) als dekadischen Schwächungskoeffizienten in cm^{-1}, so findet man folgenden empirischen Zusammenhang zwischen μ_{dek} und U:

$$\mu_{dek} = \frac{\mu_0}{U} + \mu_1 = \frac{4.45 \cdot 10^{-2}}{U} + 4.00 \cdot 10^{-2} \tag{6}$$

Hiernach kann man leicht übersehen, wie sich die Erkennbarkeit von Weichteilkontrasten in Abhängigkeit von der Röhrenspannung ändert. Die durch Quadrate bezeichneten Punkte in Diagramm 5 sind aus Messwerten von NEMET, COX und HILLS (4) bestimmt worden.

3. Äquivalente Aufnahmebedingungen

Die in Abschnitt 2 mitgeteilten Ergebnisse können nun dazu benutzt werden, die Leistungsfähigkeit verschiedener Apparate-Typen miteinander zu vergleichen. Die zu vergleichenden Apparate unterscheiden sich im wesentlichen durch ihre Spannungsformen, d. h. durch die Welligkeit der Spannung. An dem einen Ende der Reihe steht der Kondensator-Apparat mit geregelter Hochspannung, Welligkeit 0 %, am anderen Ende der Vierventil-Apparat (mit dem für die vorliegende Untersuchung der Halbwellen- oder Wechselspannungs-Apparat als gleichwertig anzusehen ist, da nur die mAs-Produkte von Interesse sind, nicht dagegen Strom und Zeit einzeln) mit 100 % Welligkeit. Hier soll die Welligkeit als einziges Unterscheidungsmerkmal betrachtet werden, indem angenommen wird, dass der Zeitverlauf der Spannung stets mit genügender Genauigkeit durch aneinandergesetzte Sinusbogen dargestellt werden kann. Aufnahmen, die mit Apparaten verschiedener Spannungsformen hergestellt sind, sollen dann äquivalent genannt werden, wenn sie gleiche mittlere Schwärzung haben und gleiche Kontraste vorliegen. Beide Aufnahmen müssen also mit gleichen Belichtungsgrössen J und solchen Spannungen, dass sich gleiche Schwächungskoeffizienten ergeben, gemacht werden. Die Schwächungskoeffizienten werden bei zeitlich veränderlichen Spannungen von der Scheitelspannung U_{ow} und von der Welligkeit w abhängen. Ausserdem geht jetzt noch p ein. Es ist leicht einzusehen, dass die äquivalenten Werte von U_{ow} umso weniger von w abhängen werden, je grösser p ist, da mit wachsendem p die Belichtungsgrösse J in immer mehr zunehmendem Masse durch die mit der Scheitelspannung erzeugte Strahlung bestimmt wird. Wir bestimmen zunächst die äquivalenten Spannungen und dann die bei mit äquivalenten Spannungen

gemachten Aufnahmen erforderlichen äquivalenten Ströme. Zum Schluss wird ein Vergleich der pro Aufnahme benötigten Energien durchgeführt, sowie der Dosisbelastungen des Patienten.

a) *Äquivalente Spannungen.* Die äquivalenten Spannungen unter den verschiedenen Bedingungen werden stets auf die konstante Gleichspannung bezogen, für die der Zusammenhang zwischen Spannungshöhe und Schwächungskoeffizient durch Gleichung (6) gegeben ist. Die Belichtungsgrösse bei Gleichspannung sei J_{gl}; die Belichtungsgrösse bei Wechselspannung (unter diesem Ausdruck seien im folgenden alle pulsierenden Spannungen verschiedener Welligkeit zusammengefasst) J_w ist dann:

$$J_w = \frac{1}{t} \int_0^t J_{gl} \cdot dt \tag{7}$$

Der Schwächungskoeffizient der mit Wechselspannung erzeugten Strahlung ist:

$$\mu_w = -\frac{\delta \log J_w}{\delta f} = -\frac{1}{J_w} \cdot \frac{1}{t} \int_0^t \frac{\delta J_{gl}}{\delta f}\, dt = \frac{\int_0^t J_{gl}\, \mu_{gl}\, dt}{\int_0^t J_{gl}\, dt} \tag{8}$$

Der zeitliche Verlauf der Röhrenspannung und des Röhrenstroms sei durch die Gleichung gegeben:

$$\text{a) } U_w = U_{ow} \cdot g(t) \qquad \text{b) } i_{ow} = i_o g(t)^q \tag{9}$$

Für $g(t)$ werden wir bei der numerischen Behandlung stets die Sinusfunktion nehmen. Der Exponent q in (9b) wird durch die Röhrencharakteristik bestimmt und kann bei den modernen Drehanodenröhren *i. a.* $q = 0.5$ gesetzt werden. Mit $J_{gl} = K \cdot i_{gl} \cdot t \cdot U_{gl}^{\,p}$ wird dann aus (6) und (8)

$$\mu_w = \frac{\mu_o}{U_{ow}} \frac{\int_0^t g(t)^{p+q-1}\, dt}{\int_0^t g(t)^{p+q} dt} + \mu_1 \tag{10}$$

Aus der Äquivalenzbedingung für gleichen Bildcharakter:

$$\mu_w = \frac{\mu_o}{U_{gl}} + \mu_1 \tag{11}$$

ergibt sich dann das Verhältnis der äquivalenten Spannungen zu:

$$a = \frac{U_{ow}}{U_{gl}} = \frac{S_{p+q-1}}{S_{p+q}} \tag{12}$$

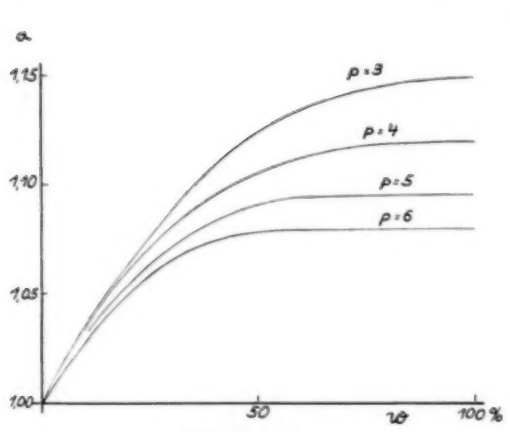

Diagramm 6.

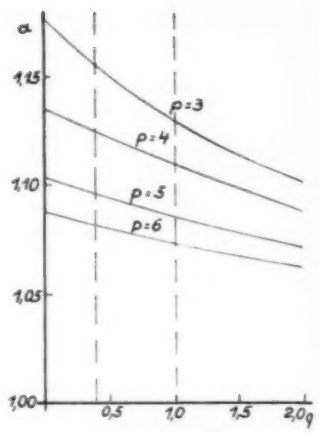

Diagramm 7.

Diagramm 6. Abhängigkeit des Spannungs-Äquivalenzfaktors von der Welligkeit (für $q = 0.5$).

Diagramm 7. Abhängigkeit des Spannungs-Äquivalenzfaktors vom Röhrendurchgriff (für $w = 100$ %).

wenn wir für die Integrale in Gleichung (10) nach Einsetzen des Sinus für $g(t)$ die Abkürzungen einführen:

$$S_n = \int_{\frac{\pi}{2}-\varphi}^{\frac{\pi}{2}} \sin^n x \cdot dx$$

dabei ist φ der Phasenwinkel, der durch die Welligkeit der Spannung bestimmt ist (für eine Welligkeit $w = 100$ % ist $\varphi = \frac{\pi}{2}$; für $w = 30$ % ist $\varphi = \frac{\pi}{4}$). In Diagramm 6 ist der Verlauf von a für verschiedene p-Werte, soweit sie für die medizinische Röntgendiagnostik in Frage kommen, als Funktion der Welligkeit aufgetragen. Die Kurve gilt für $q = 0.5$, also für übliche Diagnostikröhren mit einem relativ grossen Durchgriff (siehe 3; 6). Für Röhren mit anderen Durchgriffen sind die Äquivalenzfaktoren als Funktion von q in Diagramm 7 dargestellt. Diagr. 7 gibt dabei nur die wohl am meisten interessierenden Äquivalenzfaktoren für den Vergleich zwischen Gleichspannungs- und Vierventil-Apparaten wieder. Für Diagnostikröhren kommt dabei praktisch nur der Bereich zwischen den beiden gestrichelten Ordinaten in Frage. Kleinere Röhrendurchgriffe, d. h. grössere Werte von q können nur in gittergesteuerten Röhren erreicht

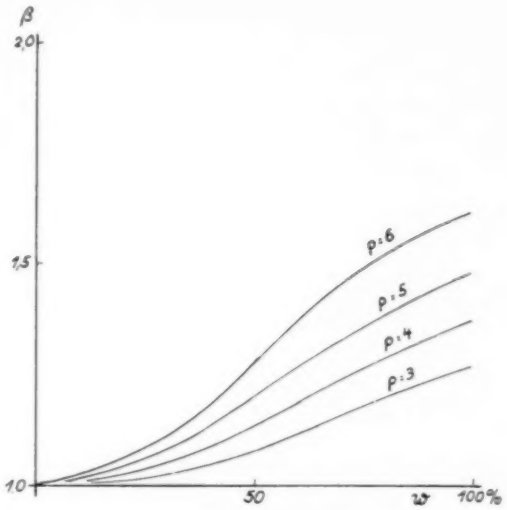

Diagramm 8.

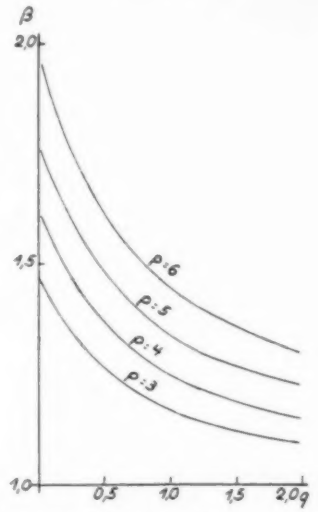

Diagramm 9.

Diagramm 8. Abhängigkeit des Strom-Äquivalenzfaktors von der Welligkeit (für $q = 0{,}5$)
Diagramm 9. Abhängigkeit des Strom-Äquivalenzfaktors vom Röhrendurchgriff (für $w = 100\ \%$).

werden. Man erkennt, worauf schon oben hingewiesen wurde, dass α umso weniger von 1 abweicht, je grösser p und je kleiner der Durchgriff ist. Die Abhängigkeit des Spannungs-Äquivalenzfaktors α von q ist, insbesonders bei grossem p, nicht bedeutend; die genaue Stromform spielt also keine wesentliche Rolle für die Bestimmung der äquivalenten Spannung.

b) *Die äquivalenten Ströme.* Die Spannungen seien zur Erzielung gleichen Bildcharakters so gewählt, dass die Scheitelwerte der Wechselspannung sich von der reinen Gleichspannung um den Faktor α nach Gleichung (12) unterscheiden. Um mit Wechselspannung eine ebenso grosse Belichtungsgrösse J am Film zu erzeugen wie mit Gleichspannung, muss das mAs-Produkt der Wechselspannungsaufnahme um den Äquivalenzfaktor β grösser sein, als das der Gleichspannungsaufnahme. Für diese Betrachtung können wir annehmen, dass beide Aufnahmen mit gleichen Zeiten geschaltet werden, so dass der Faktor β für den Röhrenstrom allein gilt:

$$\bar{i}_w = \beta \cdot i_{gl} \tag{13}$$

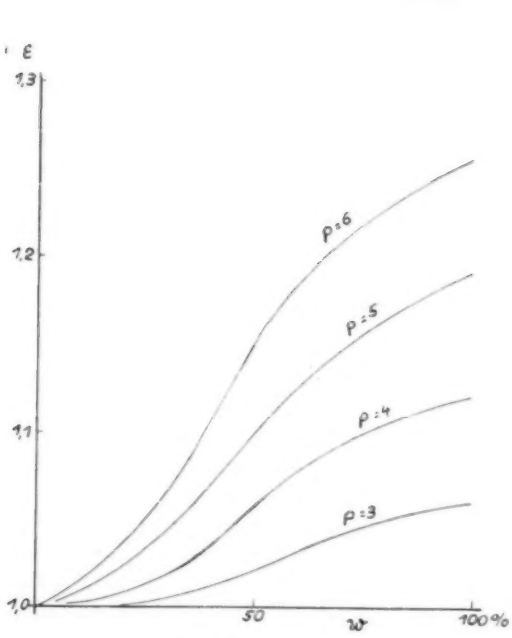

Diagramm 10.

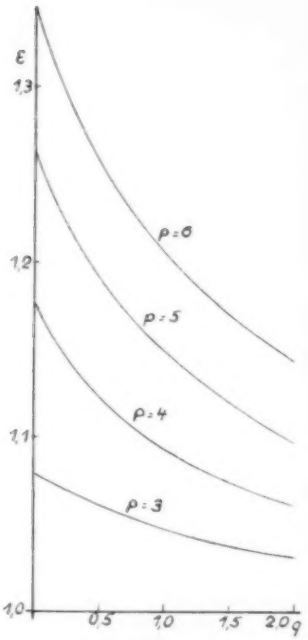

Diagramm 11.

Diagramm 10. Abhängigkeit des Energie-Äquivalenzfaktors von der Welligkeit (für $q = 0.5$).

Diagramm 11. Abhängigkeit des Energie-Äquivalenzfaktors vom Röhrendurchgriff (für $w = 100$ %).

Dabei bedeutet $\bar{i}_w$ entsprechend dem Messvorgang an den Röntgenapparaten den arithmetischen Mittelwert des Röhrenstroms, für den nach (9b) gilt:

$$\bar{i}_w = i_{ow} \cdot \frac{1}{t} \int_o^t g(t)^q \, dt \tag{14}$$

Gleichheit der Belichtungsgrössen: $J_w = J_{gl}$ bedeutet dann nach den Gleichungen (2), (7) und (9)

$$i_{gl} \cdot t \cdot U_{gl}^p = \int_o^t i_w \, U_w^p \, dt = i_{ow} \cdot U_{ow}^p \int_o^t g(t)^{p+q} \, dt \tag{15}$$

für den Strom-Äquivalenzfaktor β ergibt sich somit:

$$\beta = \frac{\bar{i}_w}{i_{gl}} = \frac{1}{a_p} \frac{S_q}{S_{p+q}} \tag{16}$$

Die Abhängigkeit des Strom-Äquivalenzfaktors β von den Grössen p, q und w ist in den Diagrammen 8 bis 9 analog zu den Diagrammen 6 bis 7 für den Spannungs-Äquivalenzfaktor dargestellt.

c) *Der Energiebedarf bei äquivalenten Aufnahmen.* Die für die Aufnahme benötigte Energie ist für Gleich-bzw. Wechselspannungen

$$E_{gl} = U_{gl} \cdot i_{gl} \cdot t \tag{17a}$$

$$E_w = \int_0^t U_w \cdot i_w \cdot dt \tag{17b}$$

Wird U_w und i_w aus den Gleichungen (9) eingesetzt, so ergibt sich unter Berücksichtigung von (14) und (16) das Verhältnis des Energiebedarfs für äquivalente Aufnahmen zu:

$$\varepsilon = \frac{E_w}{E_{gl}} = \frac{1}{\alpha^{p-1}} \cdot \frac{S_{p+1}}{S_{p+q}} \tag{18}$$

Die Diagramme 10 bis 11 zeigen die Ergebnisse der numerischen Auswertung von Gleichung (18).

d) *Die Dosisbelastung des Patienten.* Die Ausführungen in den vorhergehenden Abschnitten gestatten nun auch zahlenmässige Angaben über die Dosisbelastung des Patienten. Dabei wollen wir uns darauf beschränken, nur die Hautbelastung zu betrachten und nicht auch die Integraldosis (Volumendosis). Für den Zusammenhang zwischen der Einfallsdosis D_e, der Röhrenspannung und dem mAs-Produkt gilt in dem betrachteten Spannungsbereich die zu (2) analoge Gleichung:

$$D_e = K_e \cdot Q \cdot U^{p_e} \tag{19}$$

wobei der Spannungsexponent p_e von dem gesamten vor dem Objekt befindlichen Filter abhängt. Bei ölisolierten Röhren ist etwa $p_e \sim 1.8$. Diese Beziehung ist nicht so gut erfüllt wie Gleichung (2), doch kann die Genauigkeit als ausreichend angesehen werden. Man kann nun das Dosisverhältnis δ:

$$D_{ew} = \delta \, D_{e\,gl} \tag{20}$$

ganz analog wie den Strom-Äquivalenzfaktor β berechnen. Dabei ist nur zu berücksichtigen, dass der Spannungs-Äquivalenzfaktor α von dem durch das Objekt gegebene p, das wir auch mit p_a bezeichnen wollen, abhängt und nicht von dem für die Einfallsdosis massgeblichen p_e; so ergibt sich:

$$D_{ew} = \frac{1}{t} \int_0^t D_e \, dt = K_e \cdot \int_0^t i \; U^{p_e} \, dt \tag{21}$$

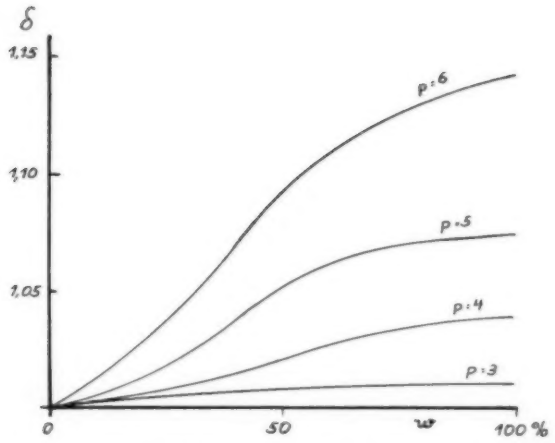

Diagramm 12. Abhängigkeit der Einfallsdosis von der Welligkeit für äquivalente Aufnahmen.

setzt man wieder U und i aus den Gleichungen (9a) und (9b) ein, so erhält man:

$$\delta = \beta \cdot a\,(p_a)^{p_e} \cdot \frac{S_{p_e+q}}{S_q} = \frac{\beta(p_a)}{\beta(p_e)} \left(\frac{a\,(p_a)}{a\,(p_e)}\right)^{p_e} \tag{22}$$

Das Dosisverhältnis δ ist also nicht so gross wie das Verhältnis der Strom-Äquivalenzfaktoren, die sich für Aufnahmen mit p_a und p_e ergeben würden, da sich der hier durchzuführende Vergleich auf die gleiche Spannungshöhe bezieht. Der Zusammenhang zwischen δ, w und p ist in Diagramm 12 dargestellt.

Ergebnisse

Aus den Aufnahmeserien mit den verschiedenen Verstärkungsfolien ergibt sich, dass bei Gleichspannungsbetrieb die Belichtungsgrösse in den Grenzen der Messgenauigkeit proportional mit einer Potenz der Röhrenspannung ist. Der Exponent liegt bei Objektdicken, die der medizinischen Praxis entsprechen, zwischen 3 und 6 und ist umso grösser, je dicker das Objekt ist. Die photographischen Schwächungskurven sind in guter Näherung Exponentialkurven. Der Schwächungskoeffizient von Wasser nimmt linear mit der Spannung ab und hat bei 120 kV etwa 2/3 des Wertes bei 50 kV.

Im folgenden wird eine Übersicht über die für äquivalente Aufnahmen

an Apparaten verschiedener Welligkeiten (w) erforderlichen Daten gegeben, bei den praktisch auftretenden Variationen der Objektdicken:

Gleich-Spannung		Drehstromapparat $w < 20$ %	4-Ventil-Apparat $w = 100$ %
Scheitelspannungen	U_{gl}	$U_{ew} < 1.05 \cdot U_{gl}$	$U_{ew} \sim 1.08 \ldots\ldots 1.15 \cdot U_{gl}$
mA-sec	Q_{gl}	$Q_w < 1.05 \cdot Q_{gl}$	$Q_w \sim 1.3 \ldots\ldots 1.6 \cdot Q_{gl}$
Energien	E_{gl}	$E_w < 1.05 \cdot E_{gl}$	$E_w \sim 1.05 \ldots\ldots 1.25 \cdot E$

Die Einfallsdosen für die Patienten unterscheiden sich bei äquivalenten Aufnahmen nicht sehr stark. Sie sind für 4-Ventil-Apparate um nicht mehr als 10 % höher als für die Gleichspannungsapparate.

ZUSAMMENFASSUNG

An Hand von Aufnahmen von Wasser-Phantomen wird dargelegt, wie sich die Belichtungsdaten für Röntgenaufnahmen mit Verstärkungsfolien mit der Spannungshöhe ändern. Aus diesen experimentellen Ergebnissen wird auf mathematischem Wege die Abhängigkeit der Belichtungsdaten von der Spannungsform abgeleitet. Die Ergebnisse der Rechnung werden in Diagrammen dargestellt. Für den Zusammenhang zwischen dem photographischen Schwächungskoeffizienten von Wasser und der Röhrenspannung wird eine empirische Formel angegeben. Die Versuche wurden mit sehr guter Streustrahlenunterdrückung durchgeführt.

SUMMARY

The effect of the variation of the tube voltage upon the exposure time in roentgenography with intensifying screens was investigated by means of measurements in water phantoms. From these experimental results it is shown that the exposure data depend on the wave form of the tube voltage. An en pirical formula is reached for the relation between the photographic absorption coefficient for water and the tube voltage. The experiment was performed with the secondary radiation efficiently suppressed.

RÉSUMÉ

L'effet de la variation de voltage du tube sur le temps de pose en radiographie avec écrans renforçateurs a été étudié par des mesures faites sur des fantômes d'eau. Ces résultats expérimentaux montrent que les facteurs d'exposition dépendent de la forme de la courbe du voltage tube. On arrive à une formule empirique reliant le coefficient d'absorption photographique de l'eau et le voltage du tube. Dans ces expériences le rayonnement secondaire avait été efficacement éliminé.

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THE EXPOSURE TIME IN ROENTGENOGRAPHY WITH SPECIAL REFERENCE TO CONDENSER DISCHARGE APPARATUS

by

Takashi Nakahori

In recent years the utilization of the condenser discharge type of roentgen apparatus has rapidly increased in Japan for the following reasons:

1. A rapid exposure is obtainable even with a small electric source. The minimum exposure time necessary for obtaining a good radiograph is limited only by the permissible loading of the roentgen tube used, and is independent of the capacity of the electric source, including the high tension transformer.

2. The exact reproduction of film density and contrast is assured.

3. Any timing device is unnecessary.

As the working conditions of the condenser discharge apparatus, however, are considerably different from those of the usual roentgen plant, its employment has presented certain problems, such as the film exposure time.

It seems to the writer that the conventional methods of measuring exposure time are unsatisfactory in the case of a condenser discharge type apparatus, and that the precise conception of exposure time in the case of the ordinary type of unit has not generally received proper consideration.

Read at the 7th International Congress of Radiology, Copenhagen, 1953; submitted for publication, 11 October 1954.

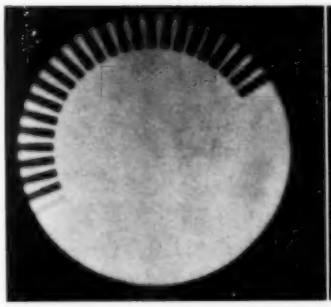

Fig. 1. Image of a lead top with a slit obtained with a full-wave rectified unit.

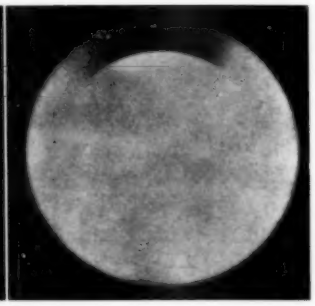

Fig. 2. Image of a lead top with a slit obtained with a condenser discharge type unit.

The exposure time in the case of a full-wave rectified unit, for example, is often checked by a roentgenogram of a lead top containing a slit, as shown in Fig. 1 and the duration τ_1, given by equation (1), is usually taken as the exposure time.

$$\tau_1 = \frac{n}{2f} \tag{1}$$

where

n: number of spots or impulses
f: frequency of electric source

However, the exact exposure time must be such a quantity as τ_2 (Diagram 1) and should be given by equation (2).

$$\tau_2 = \frac{n-1}{2f} + \Delta_1 + \Delta_2 - \Delta \tag{2}$$

where

n: number of spots or impulses which is more than 3
Δ_1: duration of the first impulse
Δ_2: duration of the last impulse
Δ: duration of each intervening impulse

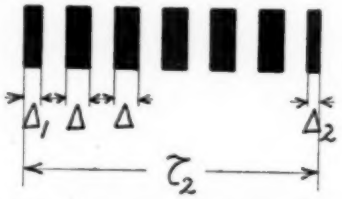

Diagram 1. Exact exposure time, τ_2, in the case of a full-wave rectified unit.

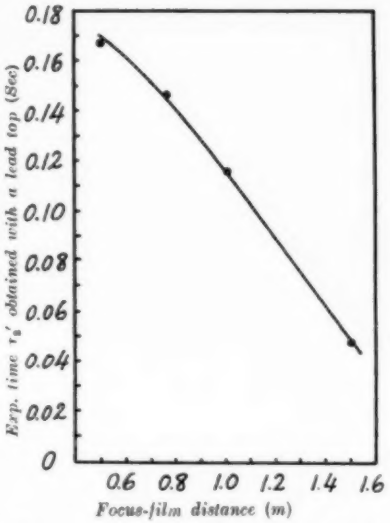

Diagram 2. An example of the relation between τ_2' and the focus-film distance.

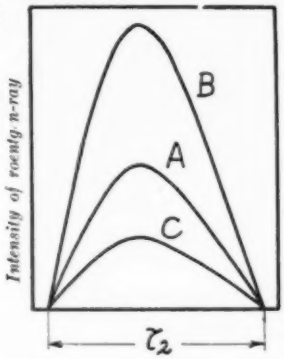

Diagram 3. Explanatory figure showing that although instantaneous intensity changes with the focus-film distance as A, B or C, the exposure time remains constant.

As the value of $(\Delta_1 + \Delta_2 - \Delta)$ is considered to be of the order of 10^{-3} sec, eq. (2) may be changed approximately into the form of eq. (3).

$$\tau_2 = \frac{n - 1}{2\,f} \tag{3}$$

There have been two conventional methods of measuring exposure time in the case of a condenser discharge type apparatus, one being the method with a lead top and the other a method in which the effective voltage is utilized.

From a radiograph of a lead top with a slit as shown in Fig. 2, the time τ_2' obtained by eq. (4) is usually taken as the exposure time.

$$\tau_2' = \frac{\theta - \theta_1}{\omega} \tag{4}$$

where

θ: angle of an image of slit
θ_1: angle of slit
ω: angular velocity of lead top

The unsuitability of the lead top method in the case of a condenser discharge type of unit is clear; the time τ_2' obtained with this method changes markedly with the focus-film distance, as shown in Diagram 2, while theoretically the exposure time τ_2 must be constant in spite of the variation of the distance, as shown in Diagram 3.

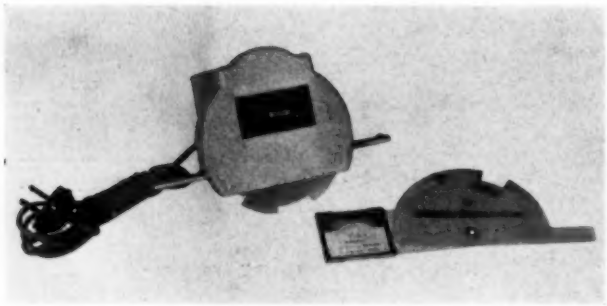

Fig. 3. Moving phantom with convenient scale to measure the unsharpness due to motion produced on film.

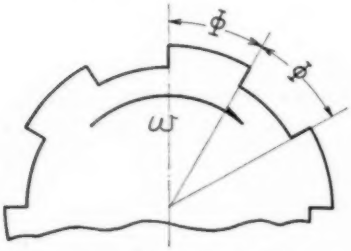

Fig. 4. Rotating aluminium disc.

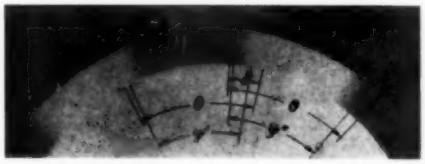

Fig. 5. Image of moving phantom taken by condenser discharge apparatus.

G. W. FILES has described effective voltage as that voltage below which no effective roentgen radiation reaches the film, and stated that he intended to take the discharging period during which the tube voltage falls from the initial value to the effective voltage as the exposure time.

This would be permissible if the effective voltage could be measured by interrupting the radiation at various voltages and inspecting the photographic effects on the film each time. Owing to the fact, however, that the effective voltage was measured as a voltage of initial charge which barely produced an image of the outline of the object, this method seems to be impracticable, complicated, and to result in error. In addition, it is necessary to measure the time required from the commencement of the discharge for the voltage to fall to this value. FILES' method has generally been employed up to now.

Returning to the starting point of this discussion, it must be pointed out that the question of the exposure time arises only because it causes unsharpness due to motion. Accordingly, it may be safely stated that the exposure time may be defined as a quantity which will be obtained by

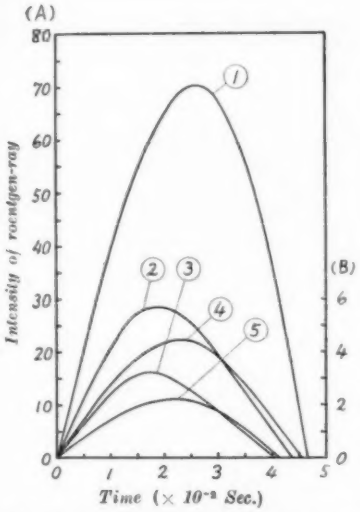

Diagram 4. Calculated examples of time-intensity curve. 1. Radiation emitted by a roentgen tube. Scale (A). 2. Radiation striking on film after passing through 6 mm Al. Scale (B). 3. Radiation through 8 mm Al. Scale (B). 4. Radiation through 10 cm paraffin. Scale (B). 5. Radiation through 10 cm paraffin + 2 mm Al. Scale (B).

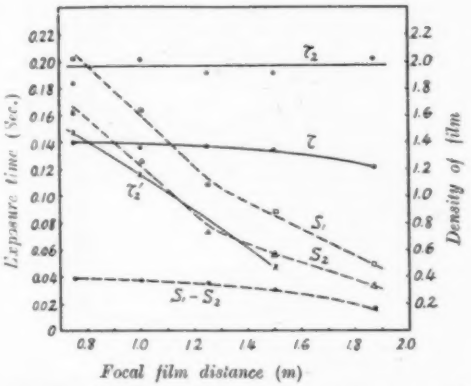

Diagram 5. Physical exposure time, τ_2, and physiologic exposure time, τ, both obtained by means of the moving phantom, and exposure time, τ_2', obtained by means of a lead top, at various focus-film distances, to the same radiation from a condenser discharge apparatus (1 μF, 50 kV, 300 mAp).

dividing the unsharpness due to motion by the speed of a moving object.

A moving phantom on this principle has been developed and is shown in Fig. 3. It consists of a rotating disc of aluminium, 2 mm in thickness, and of the shape depicted in Fig. 4. When this phantom is set between a stationary object and a film, close to the surface of the latter, any projecting sector will produce an image on the film, with unsharpness due to motion. In the case of a condenser discharge apparatus, it is necessary to use an adequate stationary phantom in addition to the moving phantom in order to obtain a reasonable exposure time; the exposure time, τ_2, changes theoretically with the kind of object radiographed, as shown in Diagram 4.

When Φ is greater than $\omega\tau_2$ (where Φ is the angle of the sector and ω the constant angular velocity of the disc) and the unsharpness produced by an edge of any moving sector will not fall on the adjacent one, the

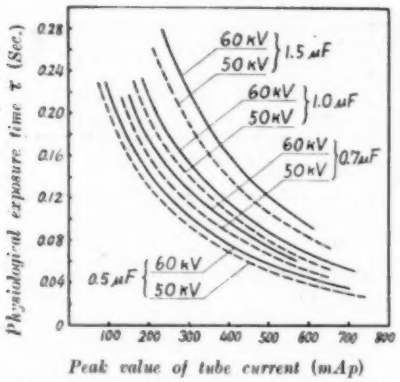

Diagram 6. Examples of physiologic exposure time, τ, of a condenser discharge apparatus; filament switching method employed.

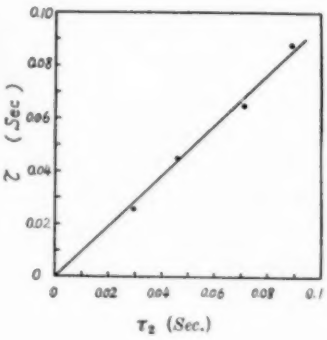

Diagram 7. Relation between τ_2 and τ in the case of a full-wave rectified unit.

exact exposure time, τ_2, will be obtained by dividing the angle of the unsharpness (shown as δ $(= \theta - \Phi)$ in Fig. 5) by the angular velocity, ω, of the sector.

Some examples of the exposure time, τ_2, obtained by measuring the unsharpness δ with a microphotometer and specified as physical exposure time, and some examples of the time, τ, obtained by measuring the unsharpness observed with the naked eye (such as $(\varphi' - \Phi)$ or $(\varphi'' - \Phi)$ in Fig. 5) and specified as physiologic exposure time, are shown in Diagram 5. These data were obtained with the same radiation emanating from a condenser discharge apparatus and directed at the film through a stationary phantom of 6 mm Al at various focus-film distances.

As to be expected theoretically, the physical exposure time, τ_2, remains constant in spite of the variation in distance. On the other hand, the physiologic exposure time, τ, changes a little with the variation in distance, and the time, τ_2' obtained from an image such as that in Fig. 2, taken with the same radiation, changes considerably, as previously described.

The difference between τ_2 and τ may be caused by the fact that some portion of both ends of the unsharpness cannot be observed with the naked eye. The tendency for τ to change with the distance may be due to the fact that the magnitude of the unobserved portion of unsharpness depends upon the density (S_1, S_2) and the contrast ($S_1 - S_2$) of the image (Diagram 5).

Concerning the choice of τ_2 or τ for practical use in roentgenographic technique, the physiologic exposure time, τ, should be chosen because

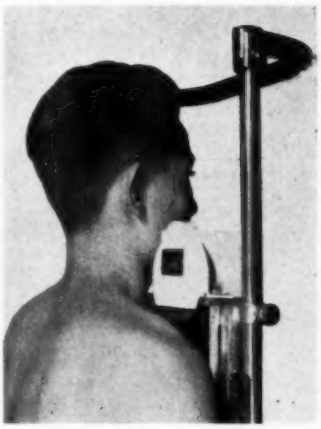

Fig. 6. Employment of the moving phantom in routine chest roentgenography.

Fig. 7. Chest roentgenogram with the image of the moving phantom in one corner

roentgen film is usually examined with the naked eye, as well as for the sake of convenience of measurement.

Some examples of τ obtained in various conditions are given in Diagram 6.

Certain experimental results of the relation between τ_2 and τ in the case of a full-wave rectified unit, where τ_2 is given by eq. (2) assuming that $\Delta_1 + \Delta_2 - \Delta = 0.004$ sec. are shown in Diagram 7.

It may be said that τ is nearly equal to τ_2 in the case of a fully rectified unit, the reason for this possibly being that the intensity of each impulse is nearly the same and fairly constant with this plant compared with a condenser discharge apparatus; accordingly, the unobserved portions of both ends of the unsharpness are negligibly small.

The employment of the moving phantom in routine chest roentgenography is shown in Fig. 6, and an example of the film obtained, with the image of the moving phantom in the corner, is depicted in Fig. 7.

Acknowledgement

The kind encouragements received from Professor M. NAKAIDZUMI and Professor K. HONDA of Tokyo University during this investigation are gratefully acknowledged.

SUMMARY

It is pointed out that the conventional conceptions or methods of measuring the exposure time in roentgenography, especially in the case of a condenser discharge type apparatus are unsatisfactory. The author suggests that the exposure time be defined as a quantity which will be obtained by dividing the unsharpness due to motion by the speed of a moving object. A moving phantom which may be used in routine chest radiography, and the data obtained with it, are described.

ZUSAMMENFASSUNG

Es wird hervorgehoben, dass die üblichen Begriffe und Methoden, die Exponierungszeit bei der Röntgenographie zu messen, nicht zufriedenstellend sind. Dieses gilt besonders bei Benutzung von Kondensatorapparaten. Der Verfasser schlägt vor, die Exponierungszeit als eine Menge zu definieren, die man durch Division der Bewegungsunschärfe mit der Geschwindigkeit des bewegten Gegenstandes erhält. Ein bewegliches Phantom kann bei der rutinemässigen Lungenphotographie benutzt werden. Die Daten, welche man auf diese Weise erhält, werden beschrieben.

RÉSUMÉ

L'auteur insiste sur le fait que les principes et les méthodes de mesure du temps de pose en radiographie, particulièrement dans le cas des appareils à décharge de condensateur, sont peu satisfaisants. Il suggère de définir le temps de pose comme la quantité obtenue en divisant le flou dû au mouvement par la vitesse d'un objet mobile. Il décrit un fantôme mobile utilisable en radiographie thoracique standard et donne les résultats obtenus avec lui.

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FROM THE RADIUM CENTRE (DIRECTOR: DR. MED. JENS NIELSEN), COPENHAGEN, DENMARK

RADIOPATHOLOGIC CYTOLOGY

The technique of Prognostic Cytology

by

Carl Deden

The effects of radiation on cells and the consequent cytoplasmic and nuclear changes have long been known although the prognostic value of these changes has not been studied until recently.

This is not the place to deal with the numerous theories regarding what occurs when ionizing rays hit cells, but it must be assumed at any rate that one of the factors is an increase in the viscosity of the latter. This is presumably the explanation why histologic preparations, and particularly smears, sometimes exhibit extremely peculiar cell shapes during and after irradiation.

In recent years, endeavours have been made to find out whether these cytologic radiation changes might be of prognostic value.

This aspect has been studied histologically during radiotherapy of carcinoma of the uterine cervix by MEIGS and PARKER (1930), FROLA (1933), ARNESON and STEWART (1935), and GLÜCKSMAN and SPEAR (1945).

Similar studies have been published by RUTH M. GRAHAM (1947), but the object of her study was vaginal secretion. It is this latter method which seems to involve most possibilities in prognostic cytology. In Denmark, investigations by ANNA MARGRETHE NIELSEN (1952) appear to confirm RUTH GRAHAM's findings.

During and after irradiation, and within a rather limited period, bizarre shapes of cells may be seen, at times with vacuolation. Such changes affect particularly the basal cells. A large number of such peculiar shapes is interpreted as a favourable prognostic sign, whereas slightly pronounced cytologic changes, or none at all, are considered prognostically bad.

Recent experience at the Radium Centre, Copenhagen, indicates that a more uniform and reliable evaluation of the cytologic radiation changes depends upon certain technical details in preparing the specimens.

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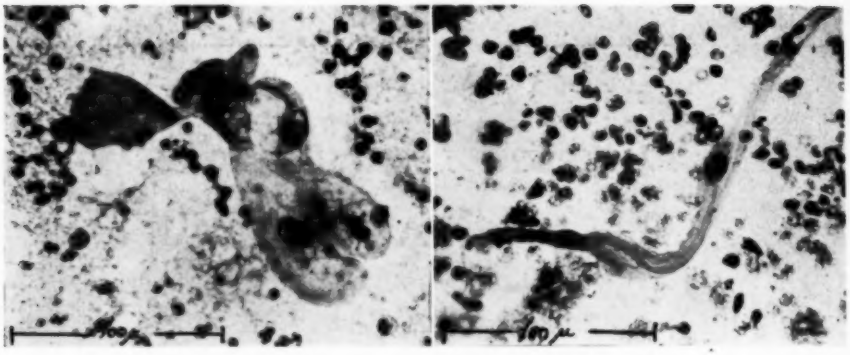

Fig. 1. Bizarre cell shapes in a vaginal smear from a patient with cervical carcinoma treated with irradiation.

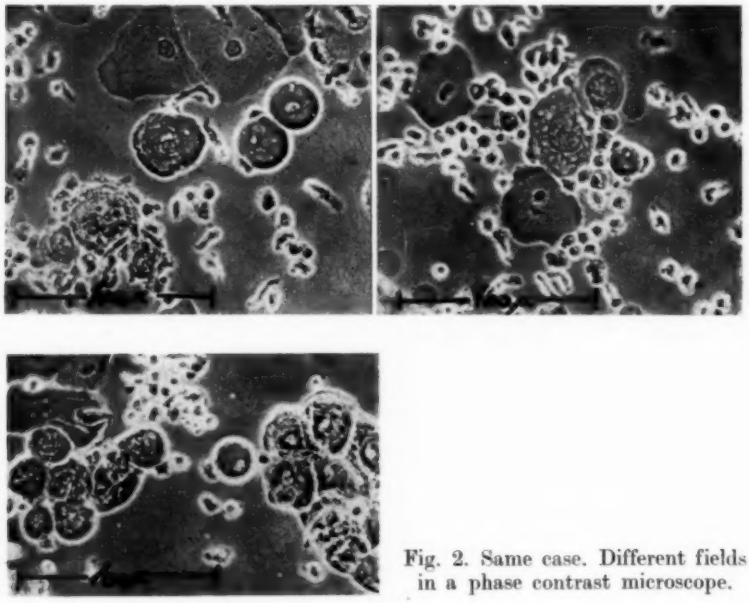

Fig. 2. Same case. Different fields in a phase contrast microscope.

It does not appear very likely that cells with changes as marked as shown in Fig. 1 really occur in the vaginal secretion, as plastic bodies usually assume a spherical shape when present in fluids.

And indeed, following suspension of the vaginal secretion in physio-

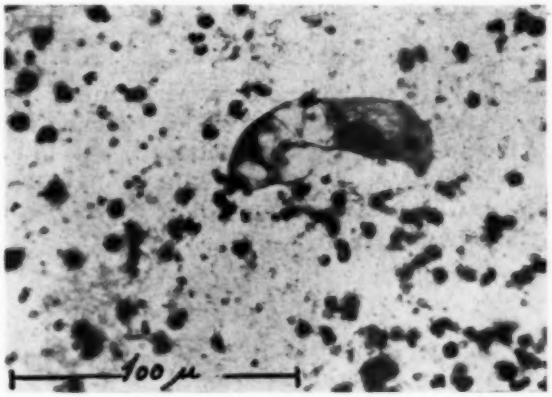

Fig. 3. Same case. Cells with vacuoles.

logic saline solution, these peculiar cell shapes were not visible in phase contrast microscopy of the wet preparation. The great majority of the cells are fairly rounded as shown in Fig. 2.

Various degrees of rough handling of the specimens in the course of smearing produce corresponding degrees of cytologic abnormalities. The cells are often elongated in the actual direction of smearing.

This seems to justify the following conclusion:

As mentioned above, the viscosity of the cells is presumably increased during irradiation. As a result, smearing may give the cells the abnormal shapes described. Even though this is an artefact, it presumably represents a response to irradiation. This seems to be the best explanation of the cell outlines seen in Fig. 1.

In a polynuclear cell, one usually expects to find the nuclei close together, but the 'elongation' of the cell may sometimes, of course, conceivably move the nuclei quite a distance apart.

Figs. 1 and 3 give the appearance that several cells, in which the vacuoles are lying close together, are coalescing.

To obtain a uniform and reliable evaluation of the prognosis by this method, it is necessary to prepare the specimens with the utmost care. On a slide smeared with egg albumin, a drop of vaginal secretion is allowed to fall from a pipette and spread by itself. If the secretion is very viscid, it should be suspended in a few drops of physiologic saline solution before being placed on the slide. As in other cytologic procedures, the specimens must be fixed before they are completely dry.

Conclusions

Though the bizarre cell shapes seen in vaginal smears during and after radiotherapy are largely artefacts, they must be presumed to represent a response to irradiation. A delicate technique, like that described above, makes the changes less marked, but will presumably in the long run ensure the preparations being more uniform and the interpretation consequently less varied. This is probably of importance, particularly in differential counts.

SUMMARY

A technique of preparing specimens with a view to a more uniform and reliable evaluation of cytologic radiation changes is described.

ZUSAMMENFASSUNG

Eine Präparationstechnik für histologische Schnitte zur Erreichung einer gleichförmigeren und zuverlässigeren Beurteilung zytologischer Strahlenschädigungen wird beschrieben.

RÉSUMÉ

L'auteur décrit une technique pour préparer les pièces, destinée à permettre une appréciation plus uniforme et plus fidèle des modifications cytologiques dues aux radiations.

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FROM THE RESEARCH INSTITUTE OF NATIONAL DEFENSE, DEPT. 1 (DIRECTOR: PROF. GUSTAF LJUNGGREN), SUNDBYBERG, SWEDEN

SLOW-NEUTRON-INDUCED RADIOACTIVITY OF SEA-WATER

by

D. Dyrssen and *P. O. Nyman*

Large numbers of fast neutrons are released in a very short period by nuclear explosions. The estimation of the activities induced by these neutrons is conveniently based on a quantitative calculation of the activities produced by 1 gram atom of slow neutrons.

No data have been reported on the activities produced in sea-water. MANDERVILLE (3) has calculated the activities obtained in filtered water from the river Schuylkill in Pennsylvania. This water contains, however, only very small quantities of salts in solution. It also seems as if MANDERVILLE has missed some negative ions by the spectrographic analysis: probably HCO_3^-, Cl^-, Br^- and SO_4^{2-}.

The sea salts of ocean water are of almost constant composition, even if there is a heavy dilution with river water. This is reflected in KNUDSEN's formula (1, p. 18, 24) correlating the salinity (salt content) to the chlorinity (chloride content).

$$S\,‰ = 0.003 + 1.805 \cdot Cl\,‰$$

The salt content is therefore to a large extent a direct measure of the composition of a water connected with sea-water (*e. g.* the Baltic). This leads to a simple relation between the induced radioactivity and the salt (or chloride) content.

Calculations

The calculations are carried out using the same principles as MANDERVILLE (3) on an artificial sea water according to LYMAN and FLEMING (1, p. 29) with a salinity of 3.45 ‰ and a chlorinity of 1.90 ‰. Furthermore, some minor constituents are added, *i. e.* those found in greater

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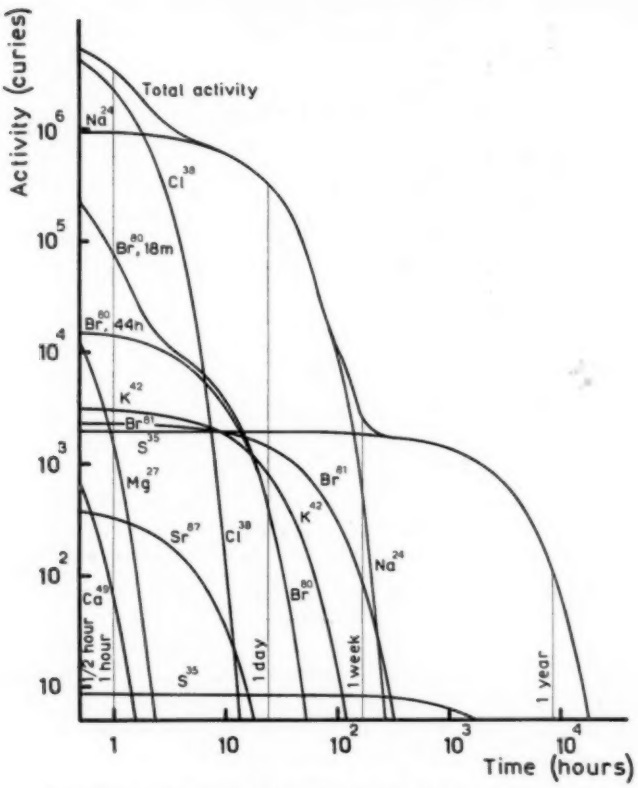

Diagram 1. Neutron-induced radioactivities in sea water.

concentration than 0.1 milligrams per liter of sea water, according to HARVEY (1, p. 31).

The number of gram atoms N′ of a particular active isotope is

$$N' = \frac{C' \cdot \sigma_{act}}{\Sigma C \cdot \sigma_{abs}}$$

where C′ is the number of gram atoms per liter of the isotope which produces the active isotope; σ_{act} and σ_{abs} are the thermal neutron cross-sections for activation and absorption according to HUGHES (2). C is the concentration of the elements in gram atoms per liter.

The activity A in curies at time zero from the same isotope is

$$A = N' \cdot \frac{6.02 \cdot 10^{23}}{3.7 \cdot 10^{10}} \cdot \frac{0.693}{t_{1/2}},$$

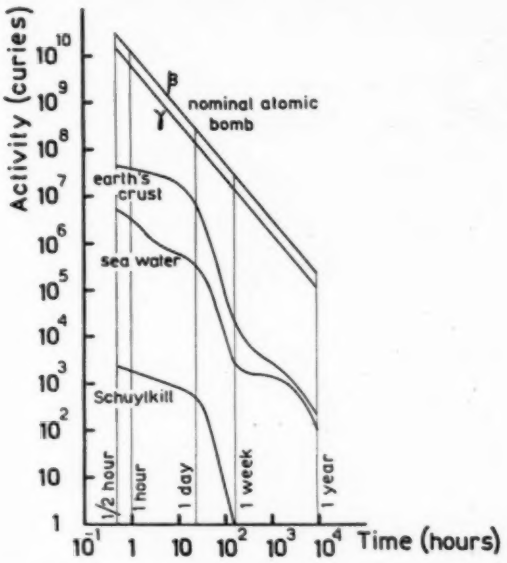

Diagram 2. Comparison between the activity of fission products and neutron-induced activities.

$t_{1/2}$ is the half-life in seconds of the activity induced. The activity at zero time (see Table I) is high for many isotopes. However, several of them are very short-lived (Li^8, B^{12}, F^{20}, Al^{28} and O^{19}) and contribute practically nothing to the total activity after half an hour. Diagram 1 shows the total activity as well as the individual activities as a function of time. As seen from Figure 1, Cl^{38} dominates during the first hours. Thereafter Na^{24} constitutes nearly the whole activity throughout the first week, after which the total activity consists mainly of S^{35} (formed from Cl^{35} through n,p-reaction). After some years, the two most active isotopes are Cl^{36} and H^3 (formed from Li^6 through n,α-reaction).

As stated above C (and C′) is proportional to the salt content S % and as the calculations in Table I have been made for S = 3.45 % the following relations are valid

$$C_S = \frac{C_{3.45} \cdot S}{3.45}; \qquad C'_S = \frac{C'_{3.45} \cdot S}{3.45}.$$

It may be seen from Table I that mainly two isotopes absorb the neutrons, namely H^1 and Cl^{35}. As the former absorption is independent of the salt content, then

$$\Sigma C_S \cdot \sigma_{abs} = 36.6 + \frac{18 \cdot S}{3.45}$$

Table I. Slow-neutron-induced

Element	Conc. in sea water gram atoms/lit.	σ_{abs} barns	$C \cdot \sigma_{abs}$	Active isotope from	% of element	C′ gram atoms/lit.	σ_{act} barns	$C' \cdot \sigma_{act}$
Li	$1.4 \cdot 10^{-5}$	70	$1.0 \cdot 10^{-3}$	Li^{6}	7.5	$1.1 \cdot 10^{-6}$	930(n,α)	$1.0 \cdot 10^{-3}$
				Li^{7}	92.5	$1.3 \cdot 10^{-5}$	$3.3 \cdot 10^{-2}$	$4.4 \cdot 10^{-7}$
B	$4.3 \cdot 10^{-4}$	750	$3.2 \cdot 10^{-1}$	B^{11}	81.2	$3.5 \cdot 10^{-4}$	$<5 \cdot 10^{-2}$	$<1.8 \cdot 10^{-5}$
C	$2.48 \cdot 10^{-3}$	$4.5 \cdot 10^{-3}$	$1.1 \cdot 10^{-5}$	C^{13}	1.1	$2.7 \cdot 10^{-5}$	$1 \cdot 10^{-3}$	$2.7 \cdot 10^{-8}$
N	$3.2 \cdot 10^{-5}$	1.78	$5.7 \cdot 10^{-5}$	N^{14}	99.6	$3.2 \cdot 10^{-5}$	1.7(n,p)	$5.4 \cdot 10^{-5}$
				N^{15}	0.37	$1.2 \cdot 10^{-7}$	$2.4 \cdot 10^{-5}$	$2.9 \cdot 10^{-12}$
F	$7.3 \cdot 10^{-5}$	$9 \cdot 10^{-3}$	$6.6 \cdot 10^{-7}$	F^{19}	100	$7.3 \cdot 10^{-5}$	$9 \cdot 10^{-3}$	$6.6 \cdot 10^{-7}$
Na ...	$4.71 \cdot 10^{-1}$	0.49	$2.3 \cdot 10^{-1}$	Na^{23}	100	$4.71 \cdot 10^{-1}$	0.54	$2.5 \cdot 10^{-1}$
Mg ...	$5.37 \cdot 10^{-2}$	$5.9 \cdot 10^{-3}$	$3.2 \cdot 10^{-3}$	Mg^{26}	11.3	$6.07 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	$3.0 \cdot 10^{-4}$
Al ...	$3.7 \cdot 10^{-5}$	0.215	$8.0 \cdot 10^{-6}$	Al^{27}	100	$3.7 \cdot 10^{-5}$	0.21	$7.8 \cdot 10^{-6}$
Si	$2.2 \cdot 10^{-5}$	0.13	$2.9 \cdot 10^{-6}$	Si^{30}	3.08	$6.8 \cdot 10^{-7}$	0.12	$8.2 \cdot 10^{-5}$
S	$2.83 \cdot 10^{-2}$	0.49	$1.4 \cdot 10^{-2}$	S^{34}	4.2	$1.19 \cdot 10^{-5}$	0.26	$3.1 \cdot 10^{-4}$
				S^{36}	0.016	$4.5 \cdot 10^{-6}$	0.14	$6.3 \cdot 10^{-7}$
Cl	$5.50 \cdot 10^{-1}$	31.6	17.4	Cl^{35}	75.4	$4.15 \cdot 10^{-1}$	0.17(n,p)	$7.1 \cdot 10^{-2}$
				Cl^{35}	75.4	$4.15 \cdot 10^{-1}$	40	16.6
				Cl^{37}	24.6	$1.35 \cdot 10^{-1}$	0.56	$7.6 \cdot 10^{-2}$
K	$9.98 \cdot 10^{-2}$	1.97	$2.0 \cdot 10^{-2}$	K^{39}	93.1	$9.29 \cdot 10^{-2}$	3	$2.8 \cdot 10^{-2}$
				K^{41}	6.9	$6.9 \cdot 10^{-4}$	1.0	$6.9 \cdot 10^{-4}$
Ca ...	$1.02 \cdot 10^{-2}$	0.43	$4.4 \cdot 10^{-3}$	Ca^{40}	96.9	$9.88 \cdot 10^{-3}$	$<1 \cdot 10^{-4}$	$<9.9 \cdot 10^{-7}$
				Ca^{44}	2.1	$2.1 \cdot 10^{-4}$	0.63	$1.3 \cdot 10^{-4}$
				Ca^{48}	0.18	$1.8 \cdot 10^{-5}$	1.1	$2.0 \cdot 10^{-5}$
Br ...	$8.28 \cdot 10^{-4}$	6.5	$5.4 \cdot 10^{-3}$	Br^{79}	50.5	$4.2 \cdot 10^{-4}$	2.9	$1.2 \cdot 10^{-3}$
				Br^{79}	50.5	$4.2 \cdot 10^{-4}$	8.5	$3.6 \cdot 10^{-3}$
				Br^{81}	49.5	$4.1 \cdot 10^{-4}$	3.5	$1.4 \cdot 10^{-3}$
Sr	$1.5 \cdot 10^{-4}$	1.16	$1.7 \cdot 11^{-4}$	Sr^{84}	0.55	$8.3 \cdot 10^{-7}$	?	?
				Sr^{86}	9.8	$1.5 \cdot 10^{-5}$	1.3	$2.0 \cdot 10^{-5}$
				Sr^{88}	82.7	$1.2 \cdot 10^{-4}$	$5 \cdot 10^{-3}$	$6.2 \cdot 10^{-7}$
H	111	0.330	36.6	H^{2}	0.015	$1.67 \cdot 10^{-2}$	$0.57 \cdot 10^{-3}$	$9.5 \cdot 10^{-6}$
O	55.5	$<2 \cdot 10^{-4}$	$<1.1 \cdot 10^{-2}$	O^{17}	0.037	$2.05 \cdot 10^{-3}$	0.5(n,α)	$1.0 \cdot 10^{-2}$
				O^{18}	0.20	$1.1 \cdot 10^{-1}$	$0.21 \cdot 10^{-3}$	$2.3 \cdot 10^{-5}$
Totals			54.6					

The total activity, $A_{S,\,tot}$, varies then with the salt content according to

$$A_{S,\,tot} = A_{3.45,\,tot} \cdot \frac{S}{3.45} \cdot \frac{54.6}{36.6 + \frac{18 \cdot S}{3.45}}$$

It may be safe to state that this relation is valid if $S > 0.1$ ‰, provided the water can be regarded as sea-water diluted with water containing only small quantities of salts. All activities of course are proportional to the number of grams of neutrons emitted in the water.

radioactivities in sea-water

Active isotope	Half-life	Activity in curies					
		at time 0	after $^1/_2$ h	after 1 h	after 1 d	after 1 week	after 1 y
H^3	12 y	$5.6 \cdot 10^{-1}$	$5.6 \cdot 10^{-1}$	$5.6 \cdot 10^{-1}$	$5.6 \cdot 10^{-1}$	$5.6 \cdot 10^{-1}$	$5.3 \cdot 10^{-1}$
Li^8	0.9 s	$1.0 \cdot 10^5$	—	—	—	—	—
B^{12}	0.03 s	$<1.2 \cdot 10^5$	—	—	—	—	—
C^{14}	5800 y	$3.1 \cdot 10^{-8}$	$3.1 \cdot 10^{-8}$	$3.1 \cdot 10^{-8}$	$3.1 \cdot 10^{-8}$	$3.1 \cdot 10^{-8}$	$3.1 \cdot 10^{-8}$
C^{14}	5800 y	$6.2 \cdot 10^{-5}$	$6.2 \cdot 10^{-5}$	$6.2 \cdot 10^{-5}$	$6.2 \cdot 10^{-5}$	$6.2 \cdot 10^{-5}$	$6.2 \cdot 10^{-5}$
N^{16}	7.4 s	$8.1 \cdot 10^{-2}$	—	—	—	—	—
F^{20}	12 s	$1.1 \cdot 10^4$	—	—	—	—	—
Na^{24}	15 h	$9.7 \cdot 10^5$	$9.5 \cdot 10^5$	$9.3 \cdot 10^5$	$3.2 \cdot 10^5$	$4.7 \cdot 10^2$	—
Mg^{27}	9.6 m	$1.1 \cdot 10^5$	$1.2 \cdot 10^4$	$1.4 \cdot 10^3$	—	—	—
Al^{28}	2.3 m	$1.2 \cdot 10^4$	—	—	—	—	—
Si^{31}	2.7 h	1.8	1.6	1.4	$3.4 \cdot 10^{-2}$	—	—
S^{35}	87 d	8.5	8.5	8.5	8.4	8.1	0.5
S^{37}	5 m	$4.4 \cdot 10^2$	6.9	$1.1 \cdot 10^{-1}$	—	—	—
S^{35}	87 d	$1.9 \cdot 10^3$	$1.9 \cdot 10^3$	$1.9 \cdot 10^3$	$1.9 \cdot 10^3$	$1.8 \cdot 10^3$	$1.1 \cdot 10^3$
Cl^{36}	$4 \cdot 10^5$	$2.8 \cdot 10^{-1}$	$2.8 \cdot 10^{-1}$	$2.8 \cdot 10^{-1}$	$2.8 \cdot 10^{-1}$	$2.8 \cdot 10^{-1}$	$2.8 \cdot 10^{-1}$
Cl^{38}	38 m	$6.9 \cdot 10^6$	$4.0 \cdot 10^6$	$2.3 \cdot 10^6$	—	—	—
K^{40}	$2 \cdot 10^9$	$9.3 \cdot 10^{-7}$	$9.3 \cdot 10^{-7}$	$9.3 \cdot 10^{-7}$	$9.3 \cdot 10^{-7}$	$9.3 \cdot 10^{-7}$	$9.3 \cdot 10^{-7}$
K^{42}	12.4 h	$3.2 \cdot 10^3$	$3.1 \cdot 10^3$	$3.0 \cdot 10^3$	$8.3 \cdot 10^2$	$2.8 \cdot 10^{-1}$	—
Ca^{45}	8.5 d	$<2.8 \cdot 10^{-1}$	$<2.8 \cdot 10^{-1}$	$<2.8 \cdot 10^{-1}$	$<2.6 \cdot 10^{-1}$	$<1.6 \cdot 10^{-1}$	—
Ca^{45}	152 d	2.1	2.1	2.1	2.0	2.0	0.4
Ca^{49}	8.5 m	$8.1 \cdot 10^3$	$7.0 \cdot 10^2$	$6.3 \cdot 10^1$	—	—	—
Br^{80}	4.4 h	$1.6 \cdot 10^4$	$1.5 \cdot 10^4$	$1.4 \cdot 10^4$	$3.6 \cdot 10^2$	—	—
Br^{80}	18 m	$6.8 \cdot 10^5$	$2.3 \cdot 10^5$	$8.1 \cdot 10^4$	$3.9 \cdot 10^2$	—	—
Br^{82}	36 h	$2.3 \cdot 10^3$	$2.3 \cdot 10^3$	$2.3 \cdot 10^3$	$1.5 \cdot 10^3$	$9.0 \cdot 10^1$	—
Sr^{85}	70 m, 65 d	?					
Sr^{87}	2.7 h	$4.3 \cdot 10^2$	$3.8 \cdot 10^2$	$3.3 \cdot 10^2$	1.0	—	—
Sr^{89}	53 d	$2.8 \cdot 10^{-2}$	$2.8 \cdot 10^{-2}$	$2.8 \cdot 10^{-2}$	$2.8 \cdot 10^{-2}$	$2.6 \cdot 10^{-2}$	$2.5 \cdot 10^{-4}$
H^3	12 y	$5.3 \cdot 10^{-3}$	$5.3 \cdot 10^{-3}$	$5.3 \cdot 10^{-3}$	$5.3 \cdot 10^{-3}$	$5.3 \cdot 10^{-3}$	$5.0 \cdot 10^{-3}$
C^{14}	5800 y	$1.2 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$
O^{19}	29 s	$1.6 \cdot 10^5$	—	—	—	—	—
			$5.22 \cdot 10^5$	$3.33 \cdot 10^6$	$3.25 \cdot 10^5$	$2.37 \cdot 10^3$	$1.10 \cdot 10^3$

In Diagram 2, $A_{3.45,\,tot}$ is compared with the gamma and beta activities emitted by the fission-products of a nominal atomic bomb (4) and with the activities induced in the earth's crust and in Schuylkill water according to MANDERVILLE (3). Diagram 3 shows the individual activities. as a function of time for the earth's crust case according to MANDERVILLE. We have corrected his values for Ca^{49} and for the Cl^{35} (n, p.) S^{35} reaction.

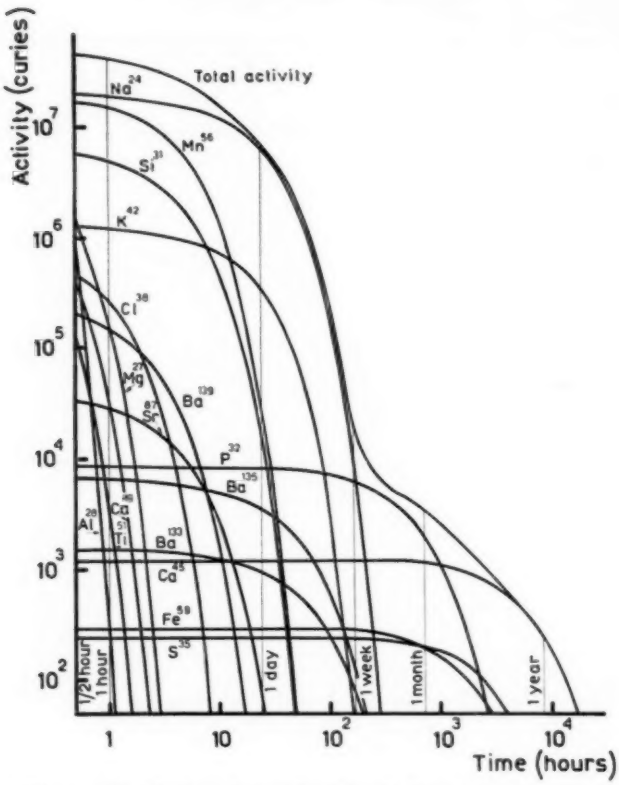

Diagram 3. Neutron-induced radioactivities in earth's crust.

It is believed that every fair judgement of the biologic effects of neutron-induced radioactivities by nuclear explosions and their relative importance compared to the effects of fission-products must be based on calculations such as those given.

SUMMARY

The radioactivity induced in sea water is calculated for 1 gram of slow neutrons. A simple relation is given for the effect of the salt content on this activity. A table shows both the total activity and the activities for individual isotopes as a function of time.

ZUSAMMENFASSUNG

Die in Meereswasser induzierte Radioaktivität wird für ein Gramm langsame Neutronen kalkuliert. Eine einfache Relation für den Effekt des Salzgehaltes auf diese Aktivität wird angegeben. Eine Tabelle zeigt die totale Aktivität sowie die Aktivitäten für individuelle Isotopen als eine Funktion der Zeit.

RÉSUMÉ

La radioactivité induite dans l'eau de mer par un gramme de neutrons lents a été calculée. Les auteurs donnent une relation simple liant la teneur en sel et la radioactivité. Une table indique l'activité totale et celle de chacun des isotopes en fonction du temps.

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BOOK REVIEW

STRAHLENDOSIS UND STRAHLENWIRKUNG. Von B. Rajewsky. 292 Seiten, 2 Abb., 79 Tafeln. Georg Thieme Verlag, Stuttgart 1954. DM 11.—.

During the last decade the rapid and extensive development of nuclear physics, particularly the production of atomic energy and huge amounts of radioactive isotopes by nuclear fission, has been accompanied by the emission of large quantities of high energy radiation, both of a corpuscular and electromagnetic nature. Like conventional roentgen radiation, and the radiation from radium, this has proved capable of serving as a valuable means of medical treatment and also of producing serious injuries. In all places where ionizing radiation is produced and used, adequate protective measures must be arranged to prevent the occurrence of such injuries.

The correlation between the biologic effect resulting from exposure to ionizing radiation, the radiation dose, and the manner in which the dose has been administered, is of fundamental importance in biophysics, radiobiology, and medical radiotherapy. This matter has consequently been the object of extensive research which has resulted in a very large number of scientific papers. They are, however, published in a variety of journals, and in different languages, and are thus not easily accessible to those who desire to collect and study the results communicated.

In the book under review, the Director of the Max-Planck Institute of Biophysics in Frankfurt a. M., Prof. B. RAJEWSKY, and members of his staff, have collected and arranged all the results considered to be valuable, well-founded, and in agreement. The material thus treated has accounted for a bibliography of more than 3,000 papers.

The book consists of three main parts, 72 pages of text, 98 pages of tables, and 112 pages of references. The main problem, 'the radiation dose and its effect', is not yet definitely solved, but is extensively illustrated in this book in an effective and interesting manner by a concentrated account of the results published. The manuscript was finished in July 1954, and the book is thus probably the most complete and modern survey of this subject available at present. It is recommended to all those who come into contact with these questions in their daily work, or who wish to obtain a résumé of the fundamental results of the research work in this branch; relevant data from atomic piles and atomic explosions are also included.

A special method of book production has effectively contributed in reducing the costs of the publication and resulted in its reasonable price.

R. Thoraeus.